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SURGERY AND WAR

ADDRESS OF THE PRESIDENT AT THE OPENING OF THE SESSION OF THE AMERICAN SURGICAL ASSOCIATION, JUNE 9, 1915

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IT is difficult, indeed impossible, for me to express my deep appreciation of the high honor of holding the position that I occupy to-day, an honor rightly shared by all the Canadian Fellows of this distinguished Scientific Association. I can only extend to you my best thanks and accompany it with a pledge to devote my best energies to the promotion of the welfare of the American Surgical Association and to do my utmost to increase its influence and power in furthering the Science and Art of Surgery and in raising its efficiency to the highest possible standard for the benefit of the people of this and the other continents. We have already accomplished much, but, if I read the signs of the times correctly, we are on the threshold of greater advances than have yet been. Greater coördination, advances in science generally, our well-equipped laboratories and improved methods of diagnosis must give the surgeon of the future a vision and a power that we older men have scarcely dreamed of.

The Canadian Fellows of this Association have always received a welcome at the meetings of the American Surgical Association that has made us feel quite at home. We one and all look forward to each annual meeting with pleasant anticipations and an assurance that the days spent in attendance will be among the most stimulating scientifically as well as enjoyable days of the year.

Last year our Association entertained the members of the Fourth Congress of the International Society of Surgery. In view of the conditions that now obtain in Great Britain and on the Continent of Europe, the remarks of the President of that Congress, Dr. de Page, have renewed interest. After reminding us that the first three meetings of the International Surgical Society had been held in Belgium, he

said, "It is not necessary for me to tell you that it is the privilege of our little Belgium to offer a meeting place to the learned men of all nationalities, covered by Europe herself with the shield of peace and liberty." I confess that I, for one, listened to his paper on War Surgery with a faraway interest.

The occurrences of the past few months, however, have brought home to us, as perhaps never before, the subject of the relation of our profession to the science and art of war, and have deprived Dr. de Page of his charming and accomplished wife who endeared herself to every member of this Association. It is now a living, vital question, and probably every member of this Association has asked himself the question, what part do Surgery and Medicine play in modern warfare? Have the means of saving life kept pace with the amazing development of those agencies used in war to destroy life?

Industrial progress, mechanical inventions, the spread of education and improved organization have greatly changed the military art. The perfection and multiplication of roads, the use of steam and gasoline, have rendered the transportation of large masses of troops, ammunition and food more rapid and less expensive in time, money and energy. Education and organization combine to render possible the movement of huge bodies of combatants in a coherent, unified mass, acting with a view to intelligent coöperation under the guidance of one supreme intellect. War is no longer a blind struggle between mobs and individuals, but a life and death struggle between educated armies led by highly trained, highly educated generals and officers. Physical stamina, courage and endurance are not less important than formerly, but intellect and nerve among the officers and in the ranks are the qualities that count most in the warfare of to-day, be it on land, in the air, on the sea, or under the water. Furthermore, intellect, education and training are as essential among the non-combatants, statesmen and politicians at home as among the combatants at the front.

War surgery of a kind is probably as old as humanity. It is safe to say that each period of the past has obtained the best surgery available at the time. Little is said of surgery and surgeons in the Old Testament. The most careful investigations have failed to make out from their writings whether the Romans regularly appointed physicians and surgeons to their armies or not, although organization has sometimes been treated very fully. Sir James Simpson, however, has established very clearly by means of monumental and votive tablets that the Romans appointed a medical officer to each cohort (500 or 600 men), and in addition, a superior medical officer or director to each legion,

which was made up of ten cohorts. In the wars of Justinian, 483–565 A.D., the recruits were examined by physicians as to their fitness. There would seem to be little doubt that the Romans made use of field hospitals, crude, no doubt, when measured by modern standards, but evidence of the humanitarian spirit that has in all centuries characterized the work of our profession. Even the American Indians had their Medicine Men.

It is a far cry from the Bowmen, and the Single Knight with mail-shirt, sword and lance to the breech-loading rifle, the machine-gun, the siege-gun, torpedo boats, submarines and air-craft, but our profession has made equally great advances and utilized all modern scientific discoveries to their fullest possibilities. If each of the succeeding wars during the ages has possessed greater engines of destruction than the one before, our profession has kept pace by producing greater instruments of relief for the sick and wounded. The science and art of surgery has kept pace with the science and art of war.

It may be said of our profession that we have given of our best. Surgeons have never hesitated to respond to their country's call in time of war, and what a galaxy of names appear down through the centuries as military surgeons. André Vesalius, Paracelsus, Ambroise Paré (1510–1590) whose presence in the army was said to be worth 10,000 men, John Hunter and Larrey, to mention only a few whose scientific work and devotion to duty are recorded on the pages of history, men who were at once a glory to their profession and a credit to their countries. Not only were these men surgeons of resource, but men of untiring energy and unbounded courage. When Larrey had no more meat with which to make broth for his sick and wounded he took the officers' horses and converted them into food. The officers quite naturally made complaints to the Emperor, who asked Larrey if the charge were true, and received the laconic answer, "Yes." Soon afterwards Napoleon made him a Baron. "History must record with admiration the answer of the French Chief of the Medical Staff when the proposal was made to him by Napoleon that the wounded be put out of their misery by opium rather than be left to the mercies of the Turks on the retreat from St. Jean d'Acre through Joffa, he replied, "My vocation is to prolong life and not to extinguish it." After the Battle of Waterloo he was captured and sentenced to be shot. Just fifteen minutes before the time set for his execution he was set free by Blucher, whose son owed his life to Larrey's exertions. At St. Helena, Napoleon wrote in his will, "I bequeath to the Surgeon-in-Chief to the French Army 100,000 francs; he is the most virtuous man I have ever known." What courage

was shown by Surgeon Landon at Majuba Hill when shot through the spine and paraplegic! He caused himself to be propped up and continued his attentions to the injured until he felt himself dying, when he simply said, " Do what you can for the wounded." During the present war Capt. Surgeon Rankin continued his attentions to the wounded after one leg had been shot away at the knee-joint. Surgeon Read, at the relief of Delhi, when the wounded under his care were threatened by a band of rebels, took his sword and, calling upon ten soldiers to follow him, defeated the enemy and saved the wounded. Two of his men were killed and five or six wounded. Surgeon Read was a Canadian and the son of a Canadian.

One might go on indefinitely with similar illustrations of the quality of the men who have served and are now serving as military surgeons. Men who fear nothing when they know they are in the right, men who have shown not less courage and determination in times of distress and danger than the brave and fearless combatant officers.

What have Scientific Medicine and Surgery done for the Army and Navy? Have they accomplished as great or greater triumphs in naval warfare and on the field of battle as in civil life in times of peace?

One hundred and fifty years ago 20 per cent., 30 per cent., 40 per cent., and sometimes 50 per cent. of the wounded died; to-day 5 per cent. or less; although many are now picked up that formerly were left to die.

Without delving too far into what Carlyle termed " dry as dust " literature, we may glance at what has been accomplished during the lifetime of some of you here present.

In the Crimean War (1854) the wounded were mixed with cases of cholera, dysentery and fever. There were no bedsteads, no proper bedding, no nurses, no washing conveniences and often only ships' biscuits for food. At best the " witches' cauldron " was brought into the middle of the ward, the patients dipped in their cups, and the bedridden were dependent on the generosity of those able to be up. Hospital gangrene was prevalent. The ever-faithful army surgeon attended the wounded in the open regardless of snow and rain. To many he could only give a word of cheer and encouragement, to others a suck from his bottle of rum as he passed among them in the darkness of the night, guided by the groans of the suffering and his small horn lamp. Every wound was septic and many of them swarming with maggots. The older surgeons were afraid of the newly-discovered chloroform. The Director-General almost forbidding its use, adding that the cries of the wounded indicated that there was no fear of syncope and that pain

was a stimulant that aided recovery. The hypodermic syringe was not yet invented. In spite of all these handicaps we are told that the men recovered remarkably well, thanks to the use of tents and abundance of fresh air. Again, the medical officers enjoyed but little independence of action; they were hampered by red tape and not allowed to perform major operations without the consent of the commanding officer.

England was stirred to its depths by the reports of the sufferings of the sick and wounded in the Crimea. On November 4, 1854, Florence Nightingale, with a staff of thirty-seven nurses, partly volunteers and partly professionals, arrived at Scutari in time to receive the Balaclava wounded. She would stand twenty hours at a stretch to see the wounded accommodated. The death-rate, which in February was as high as 42 per cent., before many months had sunk to 2 per cent. She regularly took her place in the operating room to hearten the sufferers by her presence and sympathy, and at night she would make her solitary rounds of the wards, lamp in hand, stopping here and there to speak a kindly word to some patient. Soon she had 10,000 men under her care and the general superintendence of all the hospitals on the Bosphorus. Need we wonder that her character and mission were summed up in a particularly felicitous anagram, " Flit on, cheering angel."

Great advances have been made since then. The American Civil War marked the introduction of the Ambulance System, although the wounded were, in the main, carried to the rear of the contending parties by the railway hospital. The care of the injured and the sick was much better than in any preceding war in any country. They received the benefit of anæsthesia, and the nursing was much more efficient than any that had been previously obtained. A further advance was made in the Franco-Prussian War, and again in the Boer War.

The Russo-Japanese War may be, I think, regarded as notable in that it would seem that in this war the Army Medical Officers were given a more free hand, greater independence of action and greater authority. The result was surprisingly good. In the South African War, 1899–1902, no fewer than 31,000 men were invalided home on account of typhoid fever, while in the Russo-Japanese War, 1904–1905, the incidence of infective diseases, notably typhoid fever, was reduced to a figure unparalleled in any previous war, only 3.51 per cent. of the total sickness being due to enteric diseases, and the entire deaths from infective and contagious diseases amounted to only 1.24 per cent. of the entire army in the field.

Among the Japanese soldiers operations for appendicitis, hernia, floating kidneys and gall-stones were conspicuous by their absence, and

this was attributed to their plain, rational diet, one easily digested, metabolized and assimilated. The Japanese soldier was taught how to treat his intestines and his intestines treated him with equal consideration.

Medical and Surgical science is getting a hearing only in recent years. It is no longer a voice crying in the wilderness. Governments, Armies and Navies have learned to appreciate its possibilities. They have been slow to learn that special training is as essential for the Director-General of the Army Medical Service as for the Field-Marshal, the Diplomat and the Statesman, and that here as in other spheres of activity, responsibility must be coupled with power.

Sanitary Science, unknown prior to 1700, has become one of the most efficient agencies for the prevention of sickness among troops and navies.

The Greeks and Romans had no military hospitals and, in fact, they were unknown until the time of the Crusades (twelfth century). They played but a small part in the treatment of the sick and wounded until the end of the sixteenth century, and only in the latter half of the nineteenth century did they arrive at anything like their present degree of efficiency.

Hospital ships are mentioned as long ago as 1673. In 1692 there were two hospital ships attached to each squadron. We have done not less for the navy than the army. The conditions under which Jack lived in the eighteenth century are outlined by Tobias Smollett who served as Surgeon's Mate in the *Cumberland,* which sailed from Spithead on October 26, 1740. Carlyle describes Smollett, Surgeon's Mate, as proud, soft-hearted, though somewhat stern-visaged, caustic, and indignant young gentleman. The descriptions given by Smollett in "Roderick Random" of the way in which the sick and wounded were treated is probably quite correct, although almost incredible to the present generation. In the sick berth he saw about fifty miserable, distempered wretches suspended in rows, so huddled one upon another that not more than fourteen inches of space was allowed for each with his bed and bedding, and deprived of the light of day as well as of fresh air, breathing nothing but a noisome atmosphere of the morbid steams exhaled from their own excrements and diseased bodies, devoured by vermin hatched in the filth that surrounded them and destitute of every convenience necessary to people in that helpless condition. A condition that when compared with the luxurious equipment of a modern hospital ship with its lifts, its operating theatres, its comfortable wards, its baths, its nursing sisters and its large staff of sick berth

attendants, brings clearly before us the value of the contribution of medicine to naval warfare. It is interesting to note in this connection that in addition to properly equipped ambulance trains and motor ambulances, floating hospitals capable of carrying about fifty wounded and their stretchers and attendants are being introduced in France during the present war.

It is wise to look back occasionally to the accomplishments of those who have gone before. One appreciates the value of modern surgery to the world by comparison with the conditions that obtained before the discovery of sanitary science and pathogenic germs.

Do we really do better than did our predecessors?

In the unsuccessful expedition to Porto Bello in 1726, nearly the whole of the crews of the ships were destroyed by fever three times over; 2 Admirals, 10 Captains, 50 Lieutenants and between 3000 and 4000 inferior officers and men perished without striking a blow. In the taking of Havana in 1762, the Earl of Albemarle took with him in the fleet 11,000 soldiers. Between June and the middle of October 560 men perished from wounds and 4708 from sickness. At the end of the Seven Years' War a statement was drawn up in the Annual Register for 1763, from which it appeared that in all the naval battles of that war there were but 1512 sailors and marines killed, while 133,738 had died of disease or were missing. When these figures are compared with those of the Japs in the Russo-Japanese War, which show an army of approximately 600,000 men, the entire deaths from infectious and contagious diseases were only a little over 7500, or 1.24 per cent., we gain some idea of the advance we have made and of the benefits of modern, scientific medicine and surgery.

In the Crimean War 25 per cent. of the wounded died, the majority not of their wounds but of complications such as pyæmia, erysipelas, gangrene, typhoid and typhus. In the Russian War (Russo-Turkish), 1877–1878, four times as many died of disease as of wounds. Of the wounded 12 per cent. died and of the sick 6 per cent.

In the American Civil War 14.6 per cent. of the wounded died and twice as many died from disease as from battle wounds.

In the Boer War less than 9 per cent. of the wounded died, but twice as many died of disease as of wounds.

In the Russo-Japanese War there died on the Russian side a little over 4 per cent. of the wounded and on the Japanese side 6.5 per cent.

Medicine, using the word in its larger sense, has not only reduced the death-rate from wounds, not only lowered the mortality rate by the utilization of the principles of Sanitary Science and Preventive Medi-

cine, not only insured the recovery of the sick and wounded by modern principles and methods of treatment in both medicine and surgery, but it has accomplished another great achievement, an achievement not easily expressed in figures or percentage. It has raised the morale of the army and navy. It has given the men zeal, courage, hope and confidence. This is a great thing and undoubtedly contributes very materially to the increase of valor and fighting efficiency. All praise to Paré, the Frenchman who discovered the ligature, to Morton, the American who discovered anæsthetics, and to Lister, the Englishman who discovered antiseptic surgery.

The future is full of promise. Aeroplane ambulances and aeroplane conveyances will, undoubtedly, very soon take their place in the equipment of every army and every battleship. Sanitary science and preventive medicine will become more and more efficient and the troops may always be assured that the best surgery of the day will be directed to their needs.

We may safely put aside all dreams of a millennium during which there will be no war. " Pacification is an ideal of specious and glittering beauty; yet in the long march of humanity across thousands of years or thousands of centuries, it still remains an ideal, lost in inaccessible distances, as when first it gleamed across the imagination. It has always been there. We find its traces in the Iliad and in the Sagas, in the verse of Pindar and in the profound and reflective prose of Thucydides. Livy's imagination responded to it, even when with the brush of a Veronese or a Titian he painted the wars of Rome. It informs some of the noblest passages of the Annals of Tacitus. It appears as the " Truce of God " in the Middle Ages, and in the orators of the Reformation is pronounced a malediction upon him who wages war unjustly. In the seventeenth century it is proclaimed as the ideal in the name of Religion, in the eighteenth in the name of Humanity, and in the nineteenth in the name of Commerce, Industrialism and the Progress of the working classes." (Prof. Cramb's " Germany and England," 1914.)

And yet in the twentieth century Ares, the War God, has many followers ready to contribute brute strength in their wild rage of conflict, and Enyo, the Goddess, is still able to find volunteers for the destruction of cities. The great armies, however, and in greater numbers than ever before, wear Athena's colors and carry on their warfare on approved military lines.

To the disciples of Treitschke and the younger German poets, war is a duty. It wrests Government from the weak and gives it to the strong.

" In truth there is only one way to stop war, and that is for some

great power first to disarm the whole world, and then to see to it that no one shall again take up arms. Universal tyranny may create universal peace. Nothing else will. We know, of course, all that can be said about the tyrant being an International Committee, but such an International Committee must be run by somebody and it would soon become merely a tyrant under an alias. A superimposed peace and true freedom cannot keep house together." (*The Spectator*, December 10, 1914.) And yet the war spirit is as far removed from the life and aims of the Army Medical Service as the poles. We minister to all alike. There is only one password to a military hospital and it is the same password no matter in what language it is uttered, and it is the simple words, "sick and in need." Our attitude is beautifully expressed by Oliver Wendell Holmes in the following verse:

As Life's unending column pours,
Two marshalled hosts are seen,
Two armies on the trampled shores
That Death flows back between.

One marches to the drum-beat's roll,
The wide mouth clarion's bray,
And bears upon a crimson scroll
"Our glory is to slay."

One moves in silence by the stream
With sad yet watchful eyes,
Calm as the patient planet's gleam
That walks the clouded skies.

Along its front no sabres shine,
No blood-red pennons wave;
Its banner bears the single line,
"Our duty is to save."

THE INCIDENCE OF HEREDITY AS A FACTOR IN THE CAUSATION OF GOITRE*

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In any discussion of heredity in man, the question of variation is quite as important; the biologists are by no means agreed as to the relation the one bears to the other, but the relation is so intimate that heredity and variation cannot be regarded separately. Members of a family differ from one another and variations in *their* progeny can be explained only by the prepotent domination of either parent under normal metabolic conditions. The greater the prepotency, the less the variation of type, and conversely, in the same family reversion of type marks the recessive. Inheritance presents such a variety of phenomena, that it would be an unlimited task to attempt even to epitomize the theories and proven facts which students of biology have brought forth. For the purpose of this paper we have to consider, first, what is the probable cause of goitre, and then, if possible, apply the most accepted principles of heredity as apparently evidenced in the common occurrence of goitre in several or many members of the same family.

The Probable Cause of Goitre.—Although goitre is characteristically endemic in certain localities, it is widely spread over most of the world. It is found on all geological formations. It is an accepted fact that drinking water is the intermediary through which the toxin of goitre is conveyed. This was (Blauel) proven by the Sardinian Commission about the year 1848. In a certain village of 1500 inhabitants visited, 900 goitre sufferers were found; 109 were absolute cretins; while in another village, only about one kilometre distant, the people were all strong and well. The water supply of the goitre-free district was not from the same source as that of the goitre district. The water supply of the goitre district was changed, with the result that goitre disappeared. Another example, of which I might give many, is one noted by Blauel, of a report made by the younger Bircher, as follows: In an agricultural neighborhood of Rupperswyl, in 1885, 59 per cent. of the school children were found to have goitre. In 1884 the people of this community had begun to construct a new water course. In 1889 an inspection of the school children showed 25 per cent. goitrous; in 1895, 10 per cent., and

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in 1907, only 2.5 per cent. It is a fact that there are goitre-free regions in the midst of goitre districts, and, on the other hand, isolated goitre spots in goitre-free regions. Emigrants from a goitrous into a non-goitrous district gradually eliminate goitre from their families. Immigrants from a goitre-free into a goitrous district develop goitre in the first generation, cretinism in the second,—demonstrating the increasing *toxicity*. Gaylord, referring to a report by Hancke, 1819, tells of a battalion of 300 healthy men moving into an endemic goitrous district, in which all but 70 contracted goitre, and it was found necessary to remove the regiment to a non-goitrous region, where those not too far advanced recovered,—the enlargement of the thyroid disappearing. Hancke states that in the infected region referred to, individuals who boiled the water and freed it from the precipitate which it contained, and added thereto wine and sugar, very rarely developed goitre.

Now, if goitre is produced by a toxin generated by a microörganism, how may we explain the undoubted evidences of direct heredity or predisposition? Too many thousand examples of family histories have been studied, in which *heredity* seemed the only explanation for the frequent occurrence of goitre, to doubt that such an explanation was the logical one. Many families have a predisposition to goitre; one family has been reported in which 92 members had been afflicted. Many family trees indicate that certain families show a remarkable incidence of the disease; other members show an immunity, as may be the case in tuberculosis. Dr. Maude Slye's dissections and studies seem to prove that there is probably a positive hereditary incidence in cancer; I believe *it*, as well as goitre, has a microörganism infection behind it.

Goitre has been produced experimentally in man by the drinking of milk in which was mixed the filtrate of known goitrogenous water. As a control the goitrogenous water was boiled before the filtrate was removed, and given in milk to other subjects of the experiment. No goitres were to be found in the control subjects. The incubation period in man, in experimentally produced goitre, is from 13 to 15 days.

Chemical analyses do not support the view that goitre is due to the presence or absence of certain chemical salts in the water. Neither the proportion of magnesia in the drinking water, of sulphur, or carbonate of lime, nor the content of iodine, or a lack of iodine has been confirmed as a cause of goitre. Since the discovery of radium, theories have been advanced that radio-active substances in the drinking water, particularly radio-thorium, were the exciting cause of goitre. Repin says that goitrogenous water is invariably mineral water, and holds in solution chemical ingredients, possibly salts of lime and magnesia, possi-

bly radio-active substances, which are the active principle in producing goitre. In discussing this question, McCarrison, Bircher, Breitner, Lobenhoffer, and others all think that 70° Centigrade causes water to lose its toxic properties, and that it must be some infective agent that causes goitre. The researches of the Swiss Goitre Commission (this Commission is still sitting) have proven that goitrogenous waters almost invariably show an infinitely higher bacterial content than innocuous waters, and we know that in radio-active water the bacterial content is low. McCarrison's experience agrees with that of the Swiss Goitre Commission; he states that the lime and magnesia theory is untenable,—goitre has been found in New South Wales, in villages where the only source of water supply is rain water. It is found in other villages where the water is derived from snow only, and again where distilled water is used for drinking.

Goitre has been produced in rats by feeding them with natural goitrogenous waters, viz.: those of Sumiswald and Lauterbrunnen. Pregnant animals drinking goitrogenous waters, although themselves escaping, have brought forth goitrous progeny. Goitre can be produced not only in animals, but in artificially bred trout, and has been found in fish in their natural waters. Taking these statements into consideration, it seems reasonable to concede that goitre is produced by a microörganism. Metabolic and nutritional disturbances may play some part in the irregularities of the function of the thyroid gland. The weight of evidence to date predominating is that the microörganism of goitre is introduced in drinking water as the intermediary. The toxin is most probably produced in the gastro-intestinal tract, and probably the microörganisms multiply in the intestine as a menace to the individual, and as a source of infection to others. Indeed Farrant (*Lancet*, March, 1914) goes so far as to identify the microörganism as an atypical form of B. coli. He says the mutants are usually conveyed by water. They become indigenous in the intestine, and different mutants are to be found in the fæces of cases of endemic goitre. The mutants set up an apyrexial toxæmia which stimulates the thyroid, so leading to a colloid hyperplasia, and eventually to enlargement. The whole process can be imitated, and goitre induced in guinea-pigs by feeding with small doses of the mutants. Endemic goitre is preventable by the avoidance of contaminated water. It can be cured by intestinal antiseptics—the gland returns to normal provided no degeneration has taken place.

David Marine regards endemic goitre in brook trout as due to a metabolic disturbance—the result of faulty feeding (diet of liver)—and says that it can be corrected by the feeding of whole sea fish.

Gaylord and Marsh classify goitre, in the Salmonidæ, as a carcinoma identical with endemic goitre. Their experiments show goitre in the Salmonidæ to be caused by a living organism in a way practically comparable with experimentally produced goitre in man and animals. Not only can the goitre of the Salmonidæ fish be transmitted to mammals, but it has all the phenomena of spontaneous recovery and immunity.

I have been particularly interested in the question of heredity in goitre because of some personal knowledge of families in which either a more or less direct transmission by infection was responsible for the disease, or else the disease occurred as an acquired inheritance. This acquired inheritance being the result of special chemical changes in the biophores giving rise to the development of the thyroid gland, and its relationship to the thymus, the suprarenal gland, the ovaries, pancreas, etc. In the modern sense an infectious disease cannot be inherited, and it is stated by pathologists that, "the microbe of an infectious disease cannot be a constituent of the biophore." Congenital goitre and cretinism are probably, like syphilis, of intra-uterine origin. Familial goitre, more particularly when the members of the family live in widely-separated neighborhoods in goitre-free districts, can, as must so-called hereditary syphilis, be explained as derived from "the infective state" of the parents, and is strictly an inheritance. Familial inheritance of resistance to disease, immunity, as well as the continuance of certain physical characteristics for generation after generation, is well known. This can be best explained by the Mendelian precept of dominants and recessives. It strikes me that there is a well-marked resemblance between the development of congenital goitre and congenital syphilis. Examples of mothers (women and animals, free from goitre) producing congenitally goitrous progeny, would seem to bring forth the same rule as applied in Colles's law, although the law has, in a measure, been modified by serological research. Later serological research may be able to extract a toxin showing, as in the Wassermann reaction, a latent stage of the thyroid disease.

I have been induced to consider heredity in goitre from a clinical stand-point because I have had to operate in families in which there seemed no explanation for the goitre other than heredity. Recently I have operated a mother and her three daughters for goitre, and there are more members of the family who have goitre—there being, likewise, an ancestral history of goitre. I have had somewhat similar experiences in other families. I have noted particularly a family in the practice of Dr. J. H. Cole, of Council Bluffs, Iowa; there was no familial history except that the father and mother had goitre; three

children dying in infancy, all had goitre; another infant eight days old, with a goitre threatening asphyxiation, was successfully operated by Dr. Donald Macrae; the four older living children each had a goitre. My experience teaches me that Plummer's clinical classification of goitre, based upon pathological studies, is a very important one. This classification has, I believe, a wider significance, in that it is applicable where goitre is an inheritance, or at least has an apparent hereditary cause in its formation. Particularly may this apply in the prophylactic removal of non-hyperplastic goitres before there is a development of inherited toxic properties. The disease, from a hereditary stand-point, as passed down from parent to offspring, may not be *the same* in each, because elements determining the possibility and types of growth, in one offspring may be dominant, and in another recessive, and strongly influenced by differences in metabolism.

LAPAROTOMY IN TYPHOID FEVER*

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During the last few years there has been a marked decrease in the number of cases of typhoid fever, due to our better knowledge of this disease, and hence better sanitation and more careful selection of food and drinking water. Besides this we have now an antityphoid vaccine which has rendered the disease a most uncommon one in the army, where its use is compulsory and which may in time make typhoid fever as uncommon as small-pox.

Year by year the cases of typhoid in our large hospitals are becoming fewer and fewer, but as long as any occur we are always liable to see cases in which certain accidents or complications occur, which render surgical intervention a necessity.

Much has been written of late about operation for typhoid perforation. If this serious complication is unrecognized and not operated upon, it is always fatal, and it is only by prompt recognition by the medical attendant and prompt action by the surgeon that the life of the patient can be saved. In this matter, as in so many other acute abdominal emergencies, the rule of operating before a positive diagnosis is made is a most excellent one, and a strong suspicion of perforation demands immediate action. A small pin-point perforation with very slow escape of the intestinal contents gives a different clinical picture from that of a large opening caused by the sloughing of the Peyer's patch and the overwhelming dose of the liquid poison.

Of course not all patients can be saved by early laparotomy, and many patients will die of the typhoid infection regardless of operation. An exploratory opening of the abdomen does not necessarily mean great shock or added risk. It is perfectly easy in almost any of these cases to operate with a local novocaine anæsthesia or even spinal anæsthesia. As a rule the lesion is easily recognized with comparatively little handling of the intestine, because we know pretty well where to look for such perforation.

The general practitioner has been better trained to recognize an acute appendicitis and hence surgeons can report long series of operations without a death, partly due of course to the better technic,

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but more to the fact that the surgeon is called to the case before the patient is moribund.

Some years ago the most successful operator in the world would have had a very considerable percentage of mortality even could he have used the modern methods. Only by refusing to operate upon desperate cases could his statistics have shown such favorable results as at present.

I will not enter into the discussion of the symptoms, signs of perforation, and the generally accepted indications for operation, they have been thoroughly studied and written up in the last few years. Hemorrhage, which not infrequently causes a fatal termination of the disease, has been occasionally considered a reason for opening the abdomen. I can think of no more desperate undertaking than trying to find the location of such a hemorrhage and check it by surgical means. In indirect transfusion I think we have a much more safe, rational and fully as efficient a means of saving life.

Suppuration of the gall-bladder is one of the complications that must always be borne in mind. Many years ago I had a young man brought into the hospital with no history, and as he was delirious no history could be obtained from him. The abdomen was distended and in the right upper quadrant was a large sensitive mass, the temperature was high and the man was in a desperate condition. Under primary anæsthesia the abdomen was opened, a large and almost gangrenous gall-bladder was discovered and drained; he died the next day. At autopsy it was found that he had typhoid, and that the suppurating gall-bladder was due to the typhoid infection. My medical colleagues seemed to think that it was a mistake on my part to have operated, but I assured them that though the man might possibly have recovered from his typhoid, *per se,* he certainly was killed by his gangrenous cholecystitis. Here again it is possible in most cases to open the gall-bladder and drain it as soon as the condition is recognized, without the use of a general anæsthetic.

I do not claim that all infected gall-bladders should be opened in typhoid, but we know that a very large percentage of them do become infected by the typhoid bacilli and years later we find the result in gall-stones for which we operate, but I do maintain that the gall-bladder might be explored more frequently to the advantage of the patient. Many of these remain infected for a long time after the patient has apparently recovered from the original disease. We occasionally find gall-bladders filled with pus and mucus which give pure cultures of the typhoid bacillus. Is it not possible that such patients might be the so-called carriers of the disease? It is well known that the urine

may contain typhoid bacilli long after the patient is up and about, and although the cystic duct may be so blocked that it seems impossible for any of the gall-bladder contents to pass, it is probable that a certain amount does get by and might well be a source of infection for months and even years, the organism breeding there like pin-worms in an appendix.

All carriers of the disease, like the famous "typhoid Mary," should be thoroughly examined and if bacilli are found, not in the urinary but in the intestinal tract, surgical exploration and excision of the gall-bladder should be done. It is certainly reasonable to believe that an infected gall-bladder, sidetracked as it is from the intestinal stream, could go on producing typhoid bacilli, which can be eliminated slowly, giving rise to no danger to the patient, but could be of considerable menace to all about him.

Operations during an acute stage of typhoid if properly carried out cannot add materially to the danger, and I am sure in many cases they may do good, although no perforation or other gross lesion is discovered. One of the first cases on which I operated expecting to find perforation, towards which the symptoms seemed to point, showed no intestinal opening and the abdomen was washed out with salt solution and closed; the temperature immediately began to fall and the patient recovered promptly. This result of a laparotomy has been noticed by many operators, who have seen it in the perforating and non-perforating cases as well. Is it not possible that in typhoid we may have a peritoneal sepsis without perforation, and that laparotomy and perhaps washing out with salt solution may have a beneficial effect?

There are many cases of peritoneal infection caused by the germs of septic sore throat, the pneumococcus, or the tubercle bacillus, that are cured by an early laparotomy. In a recent epidemic of septic sore throat caused by milk, I saw 5 patients with abdominal infection, 3 of these were late cases and pus was present in large quantities, they all died; the other 2 were early, showing reddened peritoneum and slight excess of free fluid, and both recovered.

During my hospital experience I tried for years to be allowed to operate on suitable cases, but until perforation was almost assuredly present the medical man would not listen to the idea. I may be entirely mistaken, but from the cases that I have seen and the experiences of other men, as they have been told to me, I can but feel that there is a group of unrecognized opportunities for surgical relief. I have few facts to support my belief, and I only make the suggestion in the hope that the profession will bear the possibilities in mind.

ACUTE APPENDICITIS OCCURRING IN THE COURSE OF TYPHOID FEVER

By Homer Gage, M.D.
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Pain, tenderness and muscular spasm located in the right iliac region, and occurring in the course of a typhoid fever, are common enough to make the differential diagnosis between typhoid and appendicitis often very difficult, and always important.

A study of the reported cases shows how easily a simple typhoid may be mistaken for an acute or subacute appendicitis.

Among the unoperated cases in which appendicitis may be said to have been only suspected, are those of Moizard, Moty, Chapenay, Giozeffi, and Fazio; beyond the presence of the above-mentioned symptoms, there would seem to be no good reason for assuming that any of them were more than simple uncomplicated typhoid.

Among the cases that were subjected to operation, those of Maurange, Muhsam, Rendu, Moty, and some of Kelly's presented no real evidence of acute inflammation of the appendix; and had the condition disclosed by operation been known beforehand, the operation would in no case have been undertaken.

I have had one similar experience myself, having operated on a young man with symptoms of acute inflammation in the right iliac region, which I thought were due to an acute appendicitis. Operation disclosed a normal appendix, and the patient went through a typical run of typhoid fever. In spite of the handicap of an unnecessary operation he recovered, but the possibility of such an error, and its possibly fatal consequences, must be ever borne in mind.

The difficulties in diagnosis have, however, been made very much greater by the discovery that the appendix does share, to a greater or less extent, in the intestinal lesions of typhoid. One of the earliest suggestions of this sort is contained in the case of Sands, reported before the New York Pathological Society in 1857. The patient died of general peritonitis caused by a perforation of the appendix, and the solitary and agminated glands of the small intestine had "the appearance which they often present in typhoid fever."

Buhl had, three years before, reported the results of autopsies in 3 cases of supposed typhoid fever, in which general peritonitis and a perforated appendix were found. A more convincing case was that of Murchison, reported in 1865, in which, in addition to extensive lesions

in the ileum and cæcum, four typical typhoid ulcerations were present in the appendix.

Moore presented 4 similar cases to the Pathological Society of London in 1883. A further contribution was made by Fitz, who in 1891 reported 167 collected cases of perforating typhoid ulcer, in 5 of which the appendix was the seat of the perforation.

Rolleston in 1898 published the results of 60 post-mortem examinations made at St. George's Hospital upon patients dying of typhoid fever, from which it appears that the appendix was swollen in 5, ulcerated in 7, and perforated in 2. He adds one case of perforation of the appendix close to the cæcum, with general intestinal ulcerations found at autopsy.

In the following year Hopfenhausen reported a study of the appendix in 30 autopsies performed during an epidemic of typhoid in St. Petersburg; and although in but 2 cases were typical typhoid ulcerations found, he found that in most of the cases the appendix shared in the pathological alterations produced by the disease in the intestinal canal—the lesion in most cases being limited to a marked cellular infiltration of its walls.

Christian found the appendix showing decided changes in 19 of 119 autopsies upon typhoid fever patients. Rostowzew, quoted by Hesse, found an abnormal condition of the mucous membrane of the appendix in 60 per cent. of the autopsies in typhoid fever, but found only one case of superficial ulceration, and in several hundred autopsies, but 4 cases of perforation.

These references to a few of the more important articles in the literature of the subject are enough to show that the appendix frequently shares in the typhoid process, and that pathological changes, amounting even to perforation, are a far from uncommon complication.

Clinically these cases are usually grouped into three classes—the first class includes those cases in which appendicitis is purely accidental, occurring concurrently with typhoid in the same individual, or in which a chronic appendicitis may be roused into activity by typhoid fever.

In the second class, the appendicitis may arise from a typhoid affection of the lymph follicles, or from an ulcer situated in the appendix. In the third, appendicitis may follow typhoid fever appearing within such a brief time after the subsidence of the fever as strongly to suggest a causal relation—a causal relationship which is, however, fairly open to more than a reasonable doubt.

The cases which occur within the first few days, or before convalescence is really assured, would seem to me to fall within the first

or second group, and the third should be left to include only those in which an interval of health has intervened between the recovery from the typhoid and the incidence of the appendicitis.

In this class would seem to belong the case referred by Stokes and Amick in the *Johns Hopkins Bulletin* for 1905, which is notable as the only reported case in which a culture of Eberth's bacillus has been found. A medical student, who had had typhoid 13 years before, was seized with a typical attack of appendicitis.

At operation the appendix was found three times its normal size, gangrenous, and about to rupture at its centre. The bacillus of typhoid was found in cultures taken from two places, and was contaminated with the bacillus pyocyaneus. His Widal was positive, but instead of pointing to a recent infection, as the authors seem inclined to believe, wouldn't it represent exactly what might be expected to occur in the case of a typhoid carrier?

In any event it illustrates what seems to me a typical instance of the so-called post-typhoid appendicitis. In this same group should be included cases in which sharp angulation or stricture has resulted from the cicatrization of a typhoid ulcer, as is set forth by Hesse, though I have found no recorded example of this form.

Of the other classes, the first represents those cases in which the appendicitis seems to be a purely accidental complication, and is best illustrated by the first and third cases reported in the very interesting paper by Perron, in the *Revue de Chirurgie* of 1905.

These were cases of acute appendicitis occurring near the end of an attack of typhoid. In neither case was there anything in the gross or microscopic appearance of the specimens to suggest a true typhoid lesion; and in both, the bacteriological examination revealed a mixed infection, without any trace of the bacillus typhosus. There is apparently no connection between the typhoid infection and the concomitant appendicitis.

The second class includes the cases of true appendicitis typhosa, in which typical typhoid ulcers are found in the appendix during the course of the fever or at autopsy.

We have already referred to the observations of Moore, Rolleston, Hesse and others, which have established the existence of typhoid lesions in the appendix at autopsy. Five illustrative cases in which the evidence was obtained at operation are quoted by Kelly—3 were from personal communications of Dr. J. B. Murphy, 1 from Dr. McMonagle, and 1 from the Johns Hopkins Hospital records—and still another case has been reported by Dr. J. N. Hall.

All of this evidence makes it very clear that typhoid changes may and do occur in the appendix, similar in appearance to those which are found in the lower part of the ileum and in the cæcum, and, further, that they give rise to an acute inflammation of the appendix that may or may not terminate in perforation.

In none of the reported cases, as far as I have been able to discover, has the presence of the typhoid bacillus been noted, except in that already referred to in the report of Stokes and Amick, and that was in a case that had had typhoid 13 years before.

In Walther's case reported in 1913, the patient's blood was negative with Eberth's bacillus and with the paratyphoid A, but strongly positive with paratyphoid B; cultures from the appendiceal abscess disclosed the presence of the same organisms.

Failure to report the presence of the true typhoid bacillus may have been simply an oversight, and is perhaps of no vital importance, but it seems to me that it makes the history of the following case of especial interest.

R. W., nineteen years old, an active athletic young man, whose family and personal histories are both good, was taken with severe headache about December 1, 1910, ten days after a possible exposure to typhoid infection. He had a high temperature when first seen, and in five days had a positive Widal reaction; he entered the Worcester City Hospital on December 7, where a second positive Widal was obtained.

Typical rose spots over chest and abdomen were present on December 11, and the spleen was readily palpable. Defervescence was gradual, and the temperature reached normal on the fifteenth, and remained so until the twentieth. At 1.30 of the morning of December 20 he awoke with severe abdominal pain, more intense in the lower right quadrant, and accompanied by a spasmodic contraction of the right rectus. He vomited once. His leucocyte count, which had been 7100 on the twelfth, and 8200 on the fourteenth, had risen at 6.30 in the morning to 14,500; at 7.30 it was 15,000; at 9.00, 18,000, at 11.30, 17,300. At 1.00 P.M. his temperature was 100° and his pulse 100.

A diagnosis of probable perforation was made, and the abdomen immediately opened. A mass was felt in the region of the appendix, in the midst of which was an ounce of thin pus, and an acutely inflamed appendix, gangrenous at one spot, and covered with a thick exudate, but unruptured. This was removed, and the convalescence was uneventful. The especial point of interest was the report of the pathologist, Dr. F. H. Baker, which I quote in full.

Specimen consists of appendix and cultures from appendix abscess. Gross examination shows appendix to be about 8 cm. in length, uniformly thickened throughout, averaging 1–2 cm. in diameter. It is acutely inflamed, with its distal third covered with a thick, dirty, grayish exudate. The blood-vessels of the serous coat are markedly distended.

There is an ulceration about 5 mm. in diameter in the mucosa about 3 cm. from the tip, which extends down to the serous covering. The lumen contains a small amount of pus and liquid fæces. Microscopical examination of sections at different levels shows an acute infection everywhere, *i.e.*, there is a marked polynuclear infiltration of all coats of the appendix.

Sections through the point of ulceration show a characteristic lesion of typhoid, *i.e.*, in the lymphoid tissue of the mucosa are areas infiltrated with endothelial leucocytes. Cultures from the appendix abscess show growths of streptococci and motile bacilli. These bacilli are transplanted on various media and identified positively as bacillus typhosus and bacillus coli.

Stained sections of the appendix showed an intense infection with non-Gram staining bacilli in mucosa, and a similar infection of streptococci throughout all structures of the appendix.

Anatomical diagnosis: Typhoid ulceration of the appendix.

In this case we have an instance of an acute gangrenous appendicitis, occurring at the beginning of convalescence from an attack of typhoid fever. Its presence in the exudate and in the walls of the appendix would seem to indicate that the bacillus of typhoid was taking at least an active part in the process, and when we take into consideration the presence of a typical typhoid ulcer, and the cases already referred to in which similar ulcerations have been found in the appendix in the course of the fever, I think we are entirely justified in regarding them all as definite and logical sequences of the intestinal infection.

I am further inclined to believe that careful pathological and bacteriological examinations would show that some, at least, of the so-called simple or accidental cases of appendicitis occurring in typhoid fever are wrongly classified; and that true typhoid appendicitis is really more common than present figures would indicate.

When the inflammation of the appendix occurs after the temperature has become normal, and the possibility of an intestinal perforation has become very small, the diagnosis is not much more difficult than in cases of simple uncomplicated appendicitis, although in my own case I operated in the expectation of finding a perforation.

The symptoms are not very unlike, and the indications for operative interference are identical. The prognosis, however, appears to be much more favorable when the lesion is in the appendix than when it is in the intestine proper, largely perhaps because there is so much less danger of fecal extravasation.

The importance of a rising white count must never be overlooked. As pointed out by Cushing in 1900, "the appearance of leucocytosis in the course of typhoid fever points toward some inflammatory complication in its early stages."

In my own case, twice within eight days the count had been 7000 and 8000, and within a few hours after the onset of the pain it rose to 14,000, then to 15,000, and, in eight hours, to 18,000. A similar rise is of course present in intestinal perforation, and in every case is usually an indication for prompt surgical interference.

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ACUTE CHOLECYSTITIS COMPLICATING TYPHOID FEVER *

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There are numerous surgical complications of typhoid fever of which acute cholecystitis is one of the more uncommon. The following case is an example of this complication.

J. J. C. entered a medical service of the Boston City Hospital, September 29, 1906, suffering from typhoid fever.

Previous History.— Negative.

Present Illness.—He had been complaining of general malaise, frontal headache, pain in joints, and weakness for a few days.

Physical Examination.—Showed a man, twenty-eight years of age, medium height and well nourished. General physical examination negative. On the abdomen were a few rose spots; spleen palpable. No abdominal spasm or tenderness.

October 7: Had shown no complications and was considered a moderately sick patient suffering from typhoid fever. This afternoon he had an intestinal hemorrhage and passed about four ounces of blood. He was given morphia and an ice bag was applied to the abdomen. Diet by mouth omitted for some hours. There was no recurrence of hemorrhage during this illness.

October 23: Up to this time nothing unusual had occurred. On this date the temperature rose to 104° from 101° on the previous day, and the pulse rose to 120. There was some general spasm of the abdominal muscles in the right half of the abdomen. Palpation revealed no mass except that the spleen could be felt. No further complication was in evidence and it is doubtful if a cholecystitis were suspected.

October 27: Patient had an attack of severe pain referred to a point just below the right costal margin, accompanied by more or less general spasm. This acute pain subsided and he complained of a dull ache over the whole abdomen.

The above notes are extracted from the medical record. I saw him in consultation about ten hours after the attack of sudden abdominal pain.

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* Read before the American Surgical Association, June 9, 1915.

Examination.—Patient emaciated and pale; general condition very poor; tongue dry and coated; peritoneal facies; abdomen generally markedly rigid; no distention; tenderness most marked in the right lower quadrant. A diagnosis of probable intestinal perforation with spreading peritonitis was made; perforation of gall-bladder was not suspected nor examined for.

Operation.—Ether. A right rectus incision was made, extending down from the level of the umbilicus. On opening the peritoneal cavity considerable bile-stained fluid escaped. Exploration showed much fibrinous exudate and light adhesions around the cæcum and the coils of small intestine in that vicinity. The usual signs of typhoid ulcers of the lower ileum were in evidence but no intestinal perforation was found. In the region of the gall-bladder were many fibrinous adhesions and it was obvious that we had to do with a perforated gall-bladder. Hence, the original incision was closed quickly and the usual one made over the gall-bladder. This organ was exposed by breaking down the adhesions, and bile-stained pus was observed escaping from a small perforation on its inferior aspect, near the cystic duct. Except at this spot, there appeared to be no gangrene of its wall. A probe was passed and no gall-stones were detected. This opening was closed with catgut sutures and covered with the stomach and colon which happened to converge at this point and were fastened there with a catgut suture to wall off the site of perforation. The fundus of this considerably enlarged gall-bladder was then opened and drained in the usual way with a tube fastened in. An additional wick of gauze was passed beneath the gall-bladder.

This patient convalesced gradually without further complication. There was some discharge of bile until December 1, and the sinus finally closed about January 1. The pus obtained from the gall-bladder was reported to be "sterile."

Historical.—In 1880 Eberth demonstrated that a certain bacillus was the cause of typhoid fever and subsequently it was discovered that it is capable of producing suppuration. As early as 1829 Louis observed a condition of acute suppuration in the gall-bladder during an attack of typhoid fever. At autopsy Futterer discovered typhoid bacilli in the gall-bladder in 1888, and two years later Gilbert and Girode found these bacilli in both the bile and the wall of the gall-bladder after cholecystectomy. In Keene's exhaustive monograph on Surgical Complications of Typhoid Fever, written in 1898, only 4 cases are recorded of operation for suppurative cholecystitis due to the typhoid bacillus.

Condition of Normal Bile.—In health it is supposed that the bile

of man and animals is sterile, and experimentation shows this to be true in animals. Bile recovered from a supposedly normal gall-bladder in man during operation for other conditions is generally found to be sterile. For example, in one series of 23 cases the bile was sterile in 18. Bile possesses very little, if any, antiseptic quality against pyogenic bacteria; on the other hand, it is found to be a fairly good culture medium for typhoid and colon bacilli. In the presence of suppurative lesions in the gastro-intestinal tract, bile frequently contains bacteria. After ligation of the common bile duct in animals, bile becomes infected. Bacteria may be present without causing any lesion of the gall-bladder, appearing in pure culture or mixed infection.

Mode of Entrance of Typhoid Bacilli; Occurrence of Typhoid Cholecystitis.—Typhoid bacilli may enter the bile by one of three routes: 1. In most instances they enter by the circulatory system passing through mucous membranes into the bile. 2. They may be excreted directly by the liver cells into the bile. 3. It is possible but improbable that they ascend the biliary ducts directly from the duodenum.

As a rule, their presence alone is not enough to cause inflammation and it is the best opinion that they are present in the bile in all cases of typhoid fever. While they are supposed to be absent from all other organs in a few weeks after the subsidence of the fever, their stay in the bile may be indefinite. Their persistence in the gall-bladder is probably due to a certain degree of chronic cholecystitis which may not give rise to clinical symptoms and signs. Occasionally such instances occur without a previously recognized attack of typhoid fever. Such patients are known as typhoid "carriers" and, of course, are dangerous to the community. Typhoid bacilli frequently remain in the gall-bladder many months and sometimes years after an attack, often in pure culture. One instance of twenty-six years is recorded.

Although bacilli are generally present in the bile during an attack of typhoid fever, they do not frequently cause an acute cholecystitis. In a large series of autopsies, where death was due to typhoid fever, 2 per cent. were complicated by cholecystitis; in a series of 2864 clinical cases, 18 are recorded as having had cholecystitis, and in another such series of 895 cases, 1⅓ per cent. were so affected. In a series of 2000 autopsies after typhoid fever at Munich, only five cases of cholecystitis were found. Hence, this is an uncommon complication.

The time of the onset is more often during the third week of the fever and occurs with decreasing frequency as the case progresses. It may come on during convalescence or during a relapse, and has been known to occur independent of any recognized attack of typhoid fever.

It may be that typhoid bacilli, unaided by other factors, are capable

of causing an acute cholecystitis, but such cases are probably exceptional. This is demonstrated by the fact that, although bacilli are believed to be present in bile in about all cases, this complication of typhoid fever is unusual. Bile stasis from any cause favors the growth of bacteria which are often found in pure culture without the presence of gall-stones. Such attacks are probably provoked by œdema, due to a certain amount of inflammation of the ducts, giving rise to biliary stasis. In other instances of acute cholecystitis complicating typhoid fever, gall-stones have been found. In one series of about 200 cases of acute typhoid cholecystitis, gall-stones were present in 20 per cent. Hence, we are led to conclude that attacks are provoked by obstruction to the escape of bile or by injury from foreign bodies in the gall-bladder.

Pathology.—The pathology does not differ from that produced by other pyogenic bacteria. We have to deal with an acute catarrhal inflammation involving, primarily, the mucous membrane of the gall-bladder and it may extend to such degree as to destroy eventually the wall of the gall-bladder. We may have a superficial inflammation of the mucosa or a more or less extensive necrosis resulting in perforation. There may be multiple ulcers of the mucosa. In most cases perforation occurs near the cystic duct, but it may take place at any point.

Symptoms.—The symptoms and signs of acute cholecystitis due to the typhoid bacillus are the same as those caused by other pyogenic bacteria, but the clinical picture may be very different. If the attack occurs during the height of the fever, it may be entirely masked by the toxic condition and stupor of the patient, and even go on to perforation of the gall-bladder before being suspected. Many mild cases occurring at this time are probably overlooked. If the attack comes on during the period of convalescence or later, the usual symptoms should be observed.

Pain in the vicinity of the gall-bladder is the first complaint, but it may be referred to the epigastrium or, less frequently, toward the right lower quadrant of the abdomen. It is more or less constant and there may be exacerbations of sharp or colicky pain. At about the same time the gall-bladder region is tender and, according to the amount of tenderness, there is a varying degree of muscle spasm over it. The above symptoms become worse as the inflammation progresses. Very often one can palpate a distended gall-bladder and it may be large enough to produce dulness. There may be nausea and vomiting. These are the early symptoms and such a condition would not be often overlooked if a careful daily routine examination were made. This should

be done in all cases and localized tenderness over the gall-bladder should make one suspicious of such a complication.

Meanwhile, certain constitutional changes may be evident. There may be chills or a sudden rise in temperature, if it had previously reached normal, or an additional elevation, if already above normal. The pulse is increased. There may be a leucocytosis of from ten to fifteen thousand and this is significant, because the leucocyte count is not increased in uncomplicated typhoid fever. Jaundice is absent unless there is common bile duct obstruction. The above is the picture of an attack of acute catarrhal cholecystitis. The symptoms may gradually subside spontaneously and complete resolution follow and, undoubtedly, many such cases occur. On the other hand, the cystic duct obstruction may persist and the nutrition of the gall-bladder wall be so interfered with as to produce necrosis which, in turn, is followed by perforation and escape of vesicular contents with or without the formation of adhesions. As a rule, a fatal peritonitis follows unoperated cases.

The signs attending the perforation may be overlooked but should not be if the case is observed with care and regularity. The perforation is generally characterized by sudden pain, often with collapse, soon to be followed by the typical signs of an acute spreading peritonitis, which need not be considered here. The symptoms attending perforation of the gall-bladder do not differ very materially from those caused by perforation of the intestine, which is both commoner and more difficult to cure and, therefore, more serious. If, however, the possibility of a cholecystitis with perforation is borne in mind, fewer errors in diagnosis will be made. On opening the abdomen the presence of bile-stained fluid will be conclusive evidence of the type of lesion.

Diagnosis.—It would seem as though an attack of acute cholecystitis ought to be detected in the majority of instances provided the patient were watched carefully for this complication. Local tenderness and spasm are the chief signs and should be somewhat in evidence notwithstanding the presence of marked toxæmia and stupor due to typhoid fever. Such complication should not escape detection after this period.

An enumeration of a list of lesions for differential diagnosis would include the following: Intestinal perforation, right-sided pulmonary lesions, gastritis, perforation of gastric or duodenal ulcer, appendicitis, acute pancreatitis, peritonitis from any cause.

Prognosis.—Because this complication is commoner during the course of the fever, it is probable that the prognosis, other things being equal, is more grave than when due to other pyogenic bacteria. Many cases of acute cholecystitis, of varying degrees of severity, resolve spon-

taneously but no one can predict the outcome in any given case. In a series of 154 cases, 25 per cent. perforated. The prognosis depends chiefly upon whether perforation takes place. With rare exceptions perforation is followed by a fatal peritonitis when the case is left unoperated. The outcome of operative interference depends upon many factors. The condition of the patient already may be grave because of the severity of the attack of fever. The lapse of time between perforation and surgical intervention is a factor of the greatest importance, as after any visceral perforation. Prognosis is better if the attack takes place in the late stage of fever and better still at a later period. Mixed infection adds to the gravity, as does also extensive cholangeitis. The mortality in the various series of operated cases of perforation as reported runs from 22 to 54 per cent.

Treatment.—The treatment of cholecystitis due to the typhoid bacillus does not differ materially from that due to other pyogenic bacteria, although the operative mortality is greater for obvious reasons. Primarily it is of the greatest importance to have this complication in mind so that, when discovered, its progress may be watched and appropriate treatment instituted. Remembering that tenderness and spasm over the region of the gall-bladder are the early and important signs, it is a very simple matter to make a daily routine examination of this area.

Operation should be avoided if possible because of the general condition of the patient and because many of the cases are mild and resolve spontaneously. If the symptoms increase in severity, it is probably the best judgment to operate. If the gall-bladder can be palpated, this means that there is distention due to obstruction of the cystic duct. If not operated upon, such a gall-bladder will probably empty itself only by perforation, and this additional complication should be avoided if possible. Hence, progress of the local signs without evidence of remission and the presence of a palpable gall-bladder are indications for interference. If perforation of the gall-bladder has taken place, life will depend, other things being equal, upon the promptness of operation.

PATHOLOGY OF SPLEENS REMOVED FOR CERTAIN ABNORMAL CONDITIONS OF THE BLOOD *

PRELIMINARY REPORT

By Louis B. Wilson
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This study is a continuation of a previous report [1] which covered the pathologic examination of 26 spleens removed at operation or autopsy in the Mayo Clinic, between November 14, 1905, and November 1, 1912, from patients on 18 of whom a more or less positive clinical diagnosis of splenic anæmia had been made, and of two "wandering spleens" removed at operation within the same period.

The present preliminary report covers the examination of 31 more spleens removed at operation, between December 3, 1912, and June 9, 1915. Further study of the several groups will be reported later. The cases have been studied clinically by Giffin,[2] whose grouping is observed in the following brief abstracts of the pathologic protocols:

GROUP I. CLINICAL DIAGNOSIS—SPLENIC ANÆMIA

Case I.—A76471. F. B.; male; aged thirty; duration of symptoms 6 months; splenectomy December 3, 1912. Weight of spleen 1520 grammes; notch distinct; marked perisplenitis over convex surface; capsule thickened; on section, tough, hard, with marked fibrosis. Microscopic examination shows diffuse hypertrophic fibrosis (chronic splenitis); pulp 1 †; lymphoid tissue 1; reticulum 4; endothelium of sinuses 1; pigment 3; amyloid degeneration 3; arteriosclerosis 3.

Case II.—A77560. M. P.; female; aged twenty-four; duration of symptoms 12 months; splenectomy December 28, 1912. Weight of spleen 1770 grammes; notch obliterated; exterior nodular; on gross section, hard, firm, tough. Microscopically, there is diffuse hypertrophic fibrosis (chronic splenitis); pulp 1; lymphoid tissue 1; reticulum 4; endothelium of sinuses 2; pigment 1; amyloid degeneration 3; arteriosclerosis 3.

Case III.—A82918. O. N. T.; male; aged thirty-three; duration of symptoms 36 months; splenectomy April 25, 1913. Weight of spleen 2000 grammes; four notches, one over tip; exterior slightly roughened; no perisplenitis; on gross section, fairly hard and tough; vessels thick-walled. Microscopic sections show diffuse hypertrophic fibrosis (chronic splenitis); pulp 1; lymphoid tissue 2; reticulum 4; endothelium of sinuses 2; pigment 1; amyloid degeneration 1; arteriosclerosis 3.

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* Read before the American Surgical Association, Rochester, Minn., June 10, 1915.

† The figures 0, 1, 2, 3, 4 indicate relative amounts.

CASE IV.—A48060. W. A. C.; male; aged thirty-four; duration of symptoms 12 months; splenectomy April 2, 1913. Weight of spleen 600 grammes; notch distinct, but not marked; surface smooth; slight perisplenitis at hilum; somewhat firm on section. Microscopically, there is diffuse fibrosis (chronic splenitis); pulp 2; lymphoid tissue 2; reticulum 3; endothelium of sinuses 3; pigment 1; amyloid degeneration 3; arteriosclerosis 1.

CASE V.—A89075. N. B. S.; male; aged thirty-five; duration of symptoms 6 (?) months; splenectomy October 10, 1913. Weight of spleen 1030 grammes; broad, flat, with well marked notch; surface slightly nodular; considerable perisplenitis; capsule thickened; on section, fairly hard and tough; amyloid changes showing grossly (sago spleen). Microscopically, there is diffuse hypertrophic fibrosis (chronic splenitis); pulp 2, œdematous; lymphoid tissue 2, œdematous; reticulum 3; endothelium of sinuses 3, œdematous; pigment none; amyloid degeneration 3; arteriosclerosis 2.

CASE VI.—A99539. A. F. D.; male; aged forty-five; duration of symptoms 48 months; splenectomy February 3, 1914. Weight of spleen 680 grammes; thin, flat; marked double notch; considerable perisplenitis; capsule thickened; cuts rather easily; gross subcapsular amyloid changes. Microscopic sections show diffuse fibrosis (chronic splenitis); pulp 1; lymphoid tissue 1; reticulum 3; endothelium of sinuses 3; pigment none; amyloid degeneration 2; arteriosclerosis 1.

CASE VII.—A109051. S. F. R.; female; aged forty-five; duration of symptoms 60 months; splenectomy July 9, 1914. Weight of spleen 560 grammes; very slight notch; gland normal in shape; exterior slightly nodular; very little perisplenitis; capsule not thickened; cuts readily; slightly harder than normal. Microscopic sections show diffuse fibrosis (chronic splenitis); pulp 1; lymphoid tissue 2; reticulum 3; endothelium of sinuses 3; pigment none; amyloid changes 1; arteriosclerosis 1.

CASE VIII.—A118388. C. H. B.; male; aged twenty-four; duration of symptoms 36 months; splenectomy November 24, 1914. Weight of spleen 900 grammes; normal symmetry; very slight notch; surface nodular; slight perisplenitis; capsule not thickened; on gross section, hard, firm, tough; marked amyloid (sago spleen); vessel walls grossly thickened. Microscopically, there is diffuse hypertrophic fibrosis (chronic splenitis); pulp 2; lymphoid tissue 2; reticulum 3; endothelium of sinuses 2; pigment 0; amyloid degeneration 4; arteriosclerosis 2.

CASE IX.—A118619. S. T.; male; aged sixteen; duration of symptoms 60 months; splenectomy November 26, 1914. Weight of spleen 875 grammes; elongated; marked notch on each margin; marked perisplenitis; capsule thickened; considerable subcapsular pigmentation in some areas; firm and hard on section. Microscopically, there is a diffuse hypertrophic fibrosis (chronic splenitis); pulp 2; lymphoid tissue 2; reticulum 4; endothelium of sinuses 2; pigment 2; amyloid degeneration 1; arteriosclerosis 2.

CASE X.—A119565. A. M.; female; aged sixty-one; duration of symptoms 12 (?) months; splenectomy December 9, 1914. Weight of spleen 500 grammes; elongated; deep single notch; slight perisplenitis; exterior slightly nodular; cuts readily; only slight increase in density. Microscopic sections show diffuse fibrosis (chronic splenitis); pulp 1; lymphoid tissue 2; reticulum 2; endothelium of sinuses 3; pigment 0; amyloid degeneration 1; arteriosclerosis 0.

CASE XI.—A115696. H. F.; female; aged forty-four; duration of symptoms 120 months; splenectomy October 21, 1914. Weight of spleen 830 grammes; elongated; multiple notches on both edges; surface roughly nodular; on gross section, cuts with some increased resistance; one large infarct; considerable amyloid degeneration. Microscopically, there is diffuse hypertrophic fibrosis (chronic splenitis); pulp 1; lymphoid tissue 2; reticulum 3; endothelium of sinuses 2; pigment 0; amyloid degeneration 2; arteriosclerosis 3.

CASE XII.—A121871. H. E.; male; aged fifty-four; duration of symptoms 8 months; splenectomy January 13, 1915. Weight of spleen 950 grammes; surface smooth; slight perisplenitis; capsule not thickened; on gross section, fairly firm; slight fibrosis. Microscopic examination shows a diffuse hypertrophic fibrosis of moderate degree (early chronic splenitis); pulp 2; lymphoid tissue 2; reticulum 2; endothelium of sinuses 2; pigment 0; amyloid degeneration 0; arteriosclerosis 2.

CASE XIII.—A77736. C. B.; male; aged twenty-six; duration of symptoms 12 months; splenectomy January 13, 1913. Weight of spleen 2290 grammes; gland broad; one small notch; surface nodular; marked perisplenitis; capsule markedly thickened; considerable amyloid (sago spleen); hemorrhages in several areas with pigmentation. Microscopic examination shows marked diffuse hypertrophic fibrosis (chronic splenitis); pulp 2; lymphoid tissue 1; reticulum 4; endothelium of sinuses 1; pigment 2; amyloid degeneration 3; arteriosclerosis 3.

CASE XIV.—A64405. M. R. C.; female; aged twenty-eight; duration of symptoms 36 months; splenectomy April 9, 1913. Weight of spleen 1346 grammes; thick, with small notch; external surface slightly roughened; considerable perisplenitis; capsule slightly thickened; one large infarct; amyloid degeneration (sago spleen). Microscopic examination shows diffuse hypertrophic fibrosis (chronic splenitis); pulp 2; lymphoid tissue 2; reticulum 3; endothelium of sinuses 1; pigment 1; amyloid degeneration 2; arteriosclerosis 0.

CASE XV.—A132194. T. K.; female; aged fifty-one; duration of symptoms 24 months; splenectomy June 9, 1915. Weight of spleen 1200 grammes; normal symmetry with marked notches both borders; surface markedly nodular; very little perisplenitis; gross section shows subcapsular amyloid degeneration. Microscopically, there is diffuse hypertrophic fibrosis (chronic splenitis); pulp 2; lymphoid tissue 2; endothelium of sinuses 2; pigment 0; amyloid degeneration 2; arteriosclerosis 1.

SUMMARY OF PROTOCOLS OF GROUP I—SPLENIC ANÆMIA

It will be seen from the above protocols that the average age of the patients with a blood picture of splenic anæmia at the time of operation was thirty-six years. The average duration of symptoms was 32 months. The average weight of the spleen was 1130 grammes. This is a little higher than the average weight (1040 grammes) of the spleens from our positive splenic anæmia (revised clinical classification) cases reported in 1913. The average of the two groups is 1093 grammes. Few of the specimens equal the weights given by Lyon,[8] who states that the average weight is 62 ounces (1860 grammes). This discrepancy is probably due to the fact that Lyon's figures are drawn

largely from autopsy reports, while ours are from operative material, the spleen continuing to enlarge until death. In general the change in the shape of the spleen is not so marked as the change in size. In other words, the hypertrophy is evenly diffuse except in those cases in which infarcts have occurred. The maintenance of the notch is important from the stand-point of clinical diagnosis.

Histologically, the most constant features are the marked reduction of the pulp and lymphoid tissue with the great increase of reticulum and the almost constant presence of amyloid degeneration and arteriosclerosis. Whether the diffuse hypertrophic fibrosis is the result of inflammatory changes, has not been accurately determined. I see no reason at present, however, to change from the commonly accepted theory that the process is one of low grade chronic inflammation. In this connection it may be noted that Bunting has isolated a diphtheroid organism in pure culture in four out of twelve tubes shown from the spleen in our Case XII.

GROUP 2. CLINICAL DIAGNOSIS—ACQUIRED PERNICIOUS ANÆMIA

CASE I.—A98774. M. S.; female; aged fifty-four; duration of symptoms 3 months; splenectomy December 11, 1914. Weight of spleen 360 grammes; normal in contour with well-marked notch; external surface slightly nodular; no perisplenitis; on gross section, cuts freely, firm but not tough. Microscopically, there is a well-marked lymphocytosis with a slight fibrosis; pulp 3; lymphoid tissue 3; reticulum 2; endothelium of sinuses 2, atrophic; pigment 1; amyloid 0; arteriosclerosis 0.

CASE II.—A112160. D. Mc.; female; aged fifty-five; duration of symptoms 24 months; splenectomy August 11, 1914. Weight of spleen 300 grammes; general contour fairly normal; small notch on each border with deep groove connecting the two; surface slightly nodular; no perisplenitis; on section, capsule not thickened; cuts readily, though firm. Microscopic examination shows a marked lymphocytosis with a slight fibrosis; pulp 2; lymphoid tissue 4; reticulum 2; endothelium of sinuses 2, atrophic; pigment 0; amyloid degeneration 0; arteriosclerosis 0.

CASE III.—A112836. D. D. B.; female; aged forty-eight; duration of symptoms 36 (?) months; splenectomy August 27, 1913. Weight of spleen 910 grammes; short, broad, thick, notch almost obliterated; surface slightly roughened; on gross section, the gland is firm, hard, tough and very dark colored. Microscopically, there is a diffuse hypertrophic fibrosis (chronic splenitis); pulp 2; lymphoid tissue 2; reticulum 3; endothelium of sinuses 2, atrophic; pigment 0; amyloid degeneration 1; arteriosclerosis 1.

CASE IV.—A124257. M. S.; male; aged twenty-six; duration of symptoms 12 months; splenectomy March 10, 1915. Weight of spleen 500 grammes; fairly normal contour, with well-marked notch; external surface smooth; no perisplenitis; on section, organ is hard though not tough. Microscopically, there is a marked lymphocytosis and moderate fibrosis; pulp 2; lymphoid tissue 4;

reticulum 2; endothelium of sinuses 2, atrophic; pigment absent; amyloid degeneration 1; arteriosclerosis 0.

Case V.—A127677. C. H.; male; aged thirty-five; duration of symptoms 3 (?) months; splenectomy April 17, 1915. Weight of spleen 186 grammes; fairly normal in contour; very slight notch; on gross section, fairly firm but not tough. Microscopically, there is a marked lymphocytosis with atrophic fibrosis; pulp 1; lymphoid tissue 4; reticulum 1; endothelium of sinuses 2, atrophic; pigment 0; amyloid degeneration 0; arteriosclerosis 0.

Case VI.—A129678. D. D. B.; female; aged forty-eight; duration of symptoms 108 months; splenectomy June 4, 1915. Weight of spleen 486 grammes; general contour thickened; external surface slightly nodular; slight perisplenitis; on gross section, capsule not thickened; organ cuts readily, though firmly; no fibrosis. Microscopically, there is a marked lymphocytosis with a slight fibrosis; pulp 2; lymphoid tissue 4; reticulum 2; endothelium of sinuses 2, atrophic; pigment 0; amyloid degeneration 0; arteriosclerosis 0.

Case VII.—A128367. J. H. D.; female; aged forty-one; duration of symptoms 3 months; splenectomy June 5, 1915. Weight of spleen 500 grammes; in contour, broad and thick with very slight notch; external surface smooth; no perisplenitis; on section, organ is firm, but not tough. Microscopically, there is a marked lymphocytosis with a moderate fibrosis; pulp 2; lymphoid tissue 3; reticulum 2; endothelium of sinuses 2; pigment absent; amyloid degeneration absent; arteriosclerosis absent.

SUMMARY OF PROTOCOLS OF GROUP 2—ACQUIRED PERNICIOUS ANÆMIA

The average age of patients with pernicious anæmia was forty-four years at the time of operation. The average duration of symptoms was 27 months. The average weight of the spleens removed was 463 grammes. Only one was less than normal (195 grammes).[4] The increase in weight is out of harmony with our conception of the atrophy usually found in the spleen in cases of pernicious anæmia.[5] Here again the discrepancy is probably accounted for by the fact that in the last stages of pernicious anæmia the spleen becomes atrophic, while our figures, based on operative cases, show an increased weight of the organ.

Cytologically the increase is mostly in the lymphoid tissue, though it is worthy of note that in one case (Case III) there was a well marked fibrosis, this spleen weighing almost twice the average weight of the glands in the series. The almost entire absence of pigment in these relatively early stage cases is again in contradiction to the usually accepted statement that in cases of pernicious anæmia the spleen is pigmented.

GROUP 3. CLINICAL DIAGNOSIS—HÆMOLYTIC ANÆMIA

Case I.—A122468. J. B. McG.; male; aged sixty-four; duration of symptoms 15 months; splenectomy January 23, 1915. Weight of spleen 1120 grammes; organ very thick with well-marked notch; external surface roughened; marked

perisplenitis; on section, capsule is not thickened; organ is hard and firm, but not tough; very pale; little amyloid. Microscopically, there is a diffuse hypertrophic fibrosis with lymphocytosis (chronic splenitis); pulp 2; lymphoid tissue 3; reticulum 3; endothelium of sinuses 2, swollen; no pigment; amyloid degeneration 2; considerable hemorrhage.

GROUP 4. CLINICAL DIAGNOSIS—SECONDARY INFECTIOUS OR SEPTIC SPLENOMEGALY

CASE I.—A107092. J. P. H.; male; aged thirty-one; duration of symptoms 3 months; splenectomy June 27, 1914. Weight of spleen 700 grammes; organ swollen; no notch; marked perisplenitis; on section, gland is fairly firm, though soft and not tough; several small infarcts. Microscopically, there is a subacute splenitis; pulp 2, necrotic; lymphoid tissue 3, swollen; reticulum 2; endothelium of sinuses 2, atrophic; pigment absent; amyloid degeneration absent; no arteriosclerosis.

GROUP 5. CLINICAL DIAGNOSIS—SYPHILIS WITH SPLENOMEGALY

CASE I.—A119102. G. H. I.; female; aged forty; duration of symptoms 24 months; splenectomy December 4, 1914. Weight of spleen 900 grammes; gland normal in contour, with very marked notch and dorsal groove; external surface slightly nodular; considerable perisplenitis; on section, organ is firm, tough and very dark colored. Microscopically, there is a diffuse fibrosis with a moderate lymphocytosis; pulp 3; lymphoid tissue 3; reticulum 3; endothelium of sinuses 2, atrophic; pigment 1; amyloid degeneration 0; arteriosclerosis 3.

CASE II.—A125899. H. S. D.; female; aged thirty-two; duration of symptoms 10 (?) months; splenectomy April 1, 1915. Weight of spleen 670 grammes; gland long and slender; no notch; slightly roughened surface; considerable perisplenitis; on gross section, organ is pale and firm, but not tough. Microscopically, there is a moderate diffuse fibrosis; pulp 2; lymphoid tissue 2; reticulum 3; endothelium of sinuses 2, swollen; pigment 0; amyloid degeneration 0; arteriosclerosis 2.

GROUP 6. CLINICAL DIAGNOSIS—HÆMOLYTIC JAUNDICE

CASE I.—A41779. J. T. G.; female; aged fifty-one; duration of symptoms 42 months; splenectomy October 28, 1913. Weight of spleen 640 grammes; gland broad, thick, with well-marked notch on each border; surface rough; considerable perisplenitis; on section, organ is pale, firm and hard. Microscopically, there is a moderate hypertrophic fibrosis; pulp 1; lymphoid tissue 2; reticulum 3; endothelium of sinuses 2; pigment 1; amyloid degeneration 0; arteriosclerosis 1.

CASE II.—A86218. A. J. H.; female; aged thirty-three; duration of symptoms 18 months; splenectomy June 30, 1913. Weight of spleen 900 grammes; elongated; very slight notch; external surface nodular; considerable perisplenitis; on gross section, organ firm, hard, but not tough. Microscopically, there is a hypertrophic fibrosis (chronic splenitis); pulp 2, swollen; lymphoid tissue 3, swollen; reticulum 3; endothelium of sinuses 2; pigment 0; amyloid degeneration 0; arteriosclerosis 1.

GROUP 7. CLINICAL DIAGNOSIS—LYMPHOSARCOMA

CASE I.—A108557. C. V.; male; aged forty-five; duration of symptoms 2 months; splenectomy July 3, 1914. Weight of spleen 1870 grammes; very broad and thick; very deep notch on border; surface rough and scarred by infarcts;

on section organ is soft and dark. Microscopically, there is a diffuse lymphosarcoma; pulp 4; lymphoid tissue 4; reticulum 1; endothelium of sinuses 1, atrophic; pigment 0; amyloid degeneration 0.

GROUP 8. CLINICAL DIAGNOSIS—ACUTE FEBRILE NON-SEPTIC (?) SPLENOMEGALY

CASE I.—A117048. L. J. L.; male; aged thirty; duration of symptoms 1 (?) month; splenectomy October 27, 1914. Weight of spleen 1940 grammes; gland swollen; slight notch; external surface smooth; some perisplenitis; on gross section, organ is soft and dark colored. Microscopically, there is a parenchymatous hyperplasia; pulp 3; lymphoid tissue 3; reticulum 1; endothelium of sinuses 3, swollen; pigment 0; amyloid degeneration 0; arteriosclerosis 0.

GROUP 9. CLINICAL DIAGNOSIS—SPLENOMEGALY WITH EOSINOPHILIA

CASE I.—A81201. F. H.; male; aged thirty-one; duration of symptoms 12 months; splenectomy July 15, 1914. Weight of spleen 2110 grammes; organ very thick, broad; well-marked notch; external surface rough; very marked perisplenitis; on section, gland is very soft. Microscopically, there is a marked parenchymatous hyperplasia; pulp 4; lymphoid tissue 2; reticulum 1; endothelium of sinuses 2, swollen; pigment 3; amyloid degeneration 0; many eosinophiles throughout splenic tissue.

GENERAL SUMMARY OF THE LAST SEVEN GROUPS

The cases of hæmolytic anæmia, lues, and hæmolytic jaundice resemble pathologically the cases of splenic anæmia. The cases of secondary infection, lymphosarcoma, acute febrile non-septic splenomegaly, and splenomegaly with eosinophilia have little pathologic relationship to either splenic anæmia or pernicious anæmia. The lymphosarcoma case is a typical lymphoma whose malignancy was shown clinically. The other three cases give the general picture of an intense acute or subacute infection, causing hypertrophy and hyperplasia of all the parenchymal elements of the spleen without material increase in the reticulum.

Our knowledge of the pathology of splenomegaly associated with chronic changes in the blood has made slow progress, largely because—except in rare instances—we have been unable to study spleens from such cases until the later or terminal stage of the diseases has been reached. Now that splenectomies are becoming more common, it is fair to assume that clinicians will be on the lookout for large spleens in all cases of pathologic conditions of the blood and that we may hope for opportunity to study early pathologic changes in the glands removed at operation. If any progress is to be made, however, we must sharply differentiate the relative changes in the various histologic elements of the spleen and these changes must be studied in correlation with accurately observed clinical phenomena. At present the clinical diagnoses of splenic anæmia, pernicious anæmia, secondary infectious anæmia,

hæmolytic jaundice, Gaucher's disease, etc., are all lacking in clearness, a condition which must be materially improved upon before an instructive parallel may be shown—if, indeed, any exist—between the several clinical syndromes in their various stages and the pathologic picture present in the spleen.

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CLINICAL NOTES ON SPLENECTOMY *

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In June 1913 I [1] published a detailed report of the clinical observations in 27 cases of splenectomy. At the present time, it is my purpose to review not in detail but only in a general way the clinical characteristics of the 58 cases of splenectomy in our Clinic since 1904. One of our patients is alive and well eight years after operation. In this instance the history was analogous to that of splenic anæmia, while the spleen showed pathologically a lymphocytic hyperplasia, not, however, with any definite evidence of malignancy. The next longest period for which a patient has remained well is seven years. In this instance there was a clinical history similar to that of splenic anæmia, while pathologically the spleen showed endothelial proliferation and the case might be said to correspond to the Gaucher type of splenic anæmia. One patient has been alive and well for six years, 2 patients have been in good health five years, 2 four years and 3 three years following operation. Pathologically the spleens in these latter cases showed a connective tissue increase with an atrophy of the Malpighian bodies.

Many types of splenomegaly are necessarily represented in this series and any classification of the cases is, of course, open to discussion and criticism. On the basis of their clinical and pathologic characteristics, they will be presented in groups as follows:

Splenectomy, April 6, 1904–June 9, 1915.

1. Splenic anæmia (pathologically diffuse fibrosis)	27 cases
2. Gaucher's disease (endothelioid hyperplasia)	3 cases [2]
3. Pernicious anæmia	7 cases
4. Hæmolytic anæmia (marked splenomegaly)	2 cases
5. Secondary infectious or septic splenomegaly	5 cases
6. Lues (marked splenomegaly)	2 cases
7. Acquired hæmolytic hæmatogenous jaundice	2 cases
8. Cirrhosis of liver	1 case
9. Myelocytic leukæmia	1 case
10. Lymphoma or lymphosarcoma	3 cases

* Read before the American Surgical Association, June 10, 1915.

[1] A complete study of the cases will appear in a series of papers upon the different types of splenomegaly.

[2] Two of these cases have been questioned. A more detailed report will be published later.

11. Tuberculosis of spleen	1 case
12. Wandering spleen	2 cases
13. Acute febrile non-septic? splenomegaly	1 case
14. Splenomegaly with marked eosinophilia	1 case
Total	58 cases

Splenic Anæmia.—In this group have been placed the 27 patients in whom the enlargement of the spleen was very great and in whom splenomegaly seemed to be the primary condition. The development of a severe type of anæmia with low color index and the absence of leukocytosis were regarded as essential. Hæmatemesis occurred in a majority of the cases. Pathologically all the spleens showed an increase of connective tissue. There were 3 operative deaths in the group, while the total number of deaths was 8 in ten years. Hemorrhage was the cause of death in 2 instances, in 1 case occurring one year after operation and in the other five and one-half years. In 3 other instances hemorrhage occurred 2 and 3 times at different periods after operation, but the patients are at present in good health. It is, therefore, evident that the patients in this group had a low operative risk and an excellent prospect of cure.

Gaucher's Disease.—Our 3 cases in which the spleen showed evidence of endothelioid hyperplasia occurred early in the series. We have been unable to obtain a history of familial tendency in any of them. One of these patients is in excellent health seven years following operation. In 2 patients the spleen had probably been enlarged since adolescence.

Pernicious Anæmia.—Seven patients with pernicious anæmia have been operated on in our clinic since August, 1914, with 1 operative death. A second patient died two months after operation with severe anæmia. The third patient, two and one-half months after operation, is in very good health with hæmoglobin at 70 per cent. In the fourth patient the condition of the blood rapidly improved after the operation and the hæmoglobin was 75 per cent. in three months. The fifth patient, nine months after operation, has gained 23 pounds, the hæmoglobin is 70 per cent. and the red blood count 3,026,000. The last 2 patients are at present in the hospital. It is therefore seen that in our small series of splenectomies for pernicious anæmia there was 1 operative death, 1 death at two months, while 3 of the patients showed marked temporary improvement. Many patients with pernicious anæmia have presented themeselves for diagnosis but we have hesitated to advise surgical treatment.

Hæmolytic Anæmia with Very Much Enlarged Spleen.—There were 2 cases of an unusual type in which the anæmia was severe in character but in which the typical count of true pernicious anæmia was not present and in which the spleen was very much larger than that ordinarily seen in pernicious anæmia. The first patient (A7040) was operated on February 10, 1910. The blood count showed a rather high color index, not, however, above 1, and there were a few mormoblasts and megaloblasts in the smears. The spleen was very large, weighing 1640 grammes. After operation showers of normoblasts occurred, a finding which is quite unusual in other types of splenomegaly save that of pernicious anæmia. The second patient was operated on January 23, 1915. The spleen was enlarged early in the history of the disease, apparently before the development of anæmia, the blood findings were similar to those of the first patient and the spleen was large, weighing 1120 grammes.

It is true that these 2 cases may in reality be pernicious anæmia, but the great size of the spleen, the fact that at no time was the blood typical of pernicious anæmia, and the further observation that the enlargement of the spleen occurred early in the disease, would rather lead to the conclusion that they belong to a separate group in the production of which a disturbance of splenic function may have been primary and in which the reaction of the bone marrow was different from that in splenic anæmia.

Secondary Infectious or Septic Splenomegaly.—Under this heading have been placed 5 cases in which the enlargement of the spleen was not marked, in which the splenomegaly did not seem to be a primary factor in the production of anæmia and in which there was evidence of preceding abdominal or systemic sepsis. One of these patients is in good health five years following operation.

Lues with Splenomegaly.—There were two instances in which large non-gummatous spleens together with secondary types of anæmia were present in patients with strong positive Wassermann reactions. In one of these the liver was smooth and specific treatment had been given elsewhere without benefit. Splenectomy was followed by marked improvement. In the other instance large palpable gummata were present in the liver. These were very much reduced by specific treatment before operation, but the size of the spleen and the degree of anæmia were not affected. In this case improvement has also been marked since splenectomy.

Acquired Hæmolytic Hæmatohepatogenous Jaundice.—Two cases have been classified as hæmolytic jaundice. It is possible that both of

them might also be regarded as advanced forms of cholangitis with cirrhosis of the liver. The chronic jaundice, however, was prominent in these patients and the anæmia was marked.

Cirrhosis of the Liver.—One case has been regarded as cirrhosis of the liver. In this patient neither was the spleen large, nor the anæmia marked. Advanced cirrhosis of the liver was found at operation.

Myelocytic Leukæmia.—A patient classified in our report of 1913 as a case of splenic anæmia and so regarded by careful observers in other clinics, but of whom it was noted at the time that the blood picture was not entirely satisfactory for this grouping, continued to be in fairly good health for five and one-half years, after which the leucocyte count became increased to 64,000 with 14 per cent. of myelocytes.

Lymphoma or Lymphosarcoma.—Our series includes 2 cases of lymphosarcoma of the spleen. One of the patients remained well for several years but finally died with generalized sarcomatosis nine years after operation. The second patient was operated on July 3, 1914, at which time there was no evidence of metastases. After operation, however, general glandular enlargement rapidly occurred and death supervened five months later. A third patient presenting a decided lymphocytic hyperplasia pathologically but no definite evidence of malignancy is well eight years after operation. This case may be benign.

Tuberculosis of the Spleen.—In 1904, a large spleen which proved to be tuberculous was removed from a patient who at the time of operation gave no definite evidence of tuberculosis elsewhere in the body.

Wandering Spleen.—Two cases of this type were operated on because of pain resulting from twisted pedicle. These patients are both alive and well three and seven years following operation.

Acute Febrile Non-septic Splenomegaly.—Several of the cases in this series were very unusual in their clinical manifestations and in the combination of conditions present. One of them was analogous in many ways to those cases occurring in Egypt and reported as Egyptian splenomegaly and deserves detailed description.

> The patient was a man, aged thirty years, who gave a history in which there was no record of previous disease. He had seemed to be toxic and somewhat stupid for 6 or 8 weeks, while a remittent fever reaching 103° had been present. There had been abdominal enlargement for only 2 weeks, but no history of hæmatemesis, while ascites was present at the time of examination and the spleen could be felt on ballottement. Wassermann test, Widal reaction, blood cultures, etc., were negative. In spite of the history of

fever and the acute course of the disease, there was no leucocytosis but a definite leucopænia with a relative increase of lymphocytes and an anæmia of the secondary type with hæmoglobin at 70 per cent. The patient remained under observation for 3 months, the condition became less acute in character, and splenectomy was finally decided on. The spleen was very large, weighing 1940 grammes, and the liver was somewhat cirrhotic. (The patient remained weak after operation, had 3 hemorrhages from the bowels, and finally died 5 months following operation.) The acute course, the presence of high fever, the rapid development of a very large spleen and ascites, the absence of leucocytosis and other evidence of sepsis and the absence of jaundice formulate the picture of a most unusual type of splenomegaly.

Splenomegaly with Marked Eosinophilia.—As far as we have been able to determine there is no case of this type to be found in the literature.

This patient was a man, aged thirty-one years. He was first seen in our Clinic in March, 1913. He had had a continued fever which was diagnosed as typhoid eight years previous, and had complained of weakness since that time. Transitory œdema had been present for ten months and had become extreme within ten days. At the time of his first visit there was a general anasarca, on account of which he was placed on milk diet, and the œdema disappeared in ten days. The blood count at that time showed a secondary type of anæmia with hæmoglobin at 69 per cent. and a leucocyte count of 15,400, while the most remarkable feature was the presence of a 66 per cent. eosinophilia. The patient was under observation for three months, during which time many blood counts were made and verified by experienced hæmatologists and the eosinophiles varied from 58 to 77 per cent. Wassermann tests were negative; stools were negative; and the examination of muscle for trichinæ was also negative, although not entirely satisfactory. The great enlargement of the spleen persisted and operation was finally decided on and performed in July, 1914. The spleen weighed 2110 grammes. The patient has done well since the operation; his leucocyte count, however, has risen to 138,000, of which from 75 to 80 per cent. are eosinophiles. There is very little basis for speculation as to the possible etiology of this unique case.

RÉSUMÉ

Our series of 58 cases includes 27 of splenic anæmia, 3 of the Gaucher type of splenic anæmia, 7 of pernicious anæmia, 2 of hæmolytic

jaundice, 5 of secondary infectious or septic splenomegaly, 2 of an unclassified type of hæmolytic anæmia with marked splenomegaly, 2 of lues, 3 of sarcoma or lymphoma, 2 wandering spleens and 1 each of myelocytic leukæmia, cirrhosis of the liver and tuberculosis of the spleen. In addition, it includes 1 case of acute febrile non-septic splenomegaly which is analogous in its clinical course to Egyptian splenomegaly, and 1 case in which splenomegaly was associated with an extremely high eosinophilic count. Splenic anæmia is, in our experience, most favorable for surgical treatment. The operative risk is relatively low and the prospect for a return to normal health excellent. Three of the 7 patients with pernicious anæmia have shown temporary improvement up to 9 months after splenectomy. Removal of the spleen in non-gummatous splenomegaly associated with syphilis has been attended with excellent results in two instances.

SURGICAL CONSIDERATIONS OF SPLENECTOMY *

By William J. Mayo, M.D.
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Splenectomy.—The safety of splenectomy depends on careful separation of the attachments of the spleen and its delivery without injury to the vascular pedicle. Therefore much depends on the size and movability of the spleen and the amount and vascularity of its adhesions as well as on the thickness of the abdominal wall.

Incision.—Bevan [1] in 1897 described a most satisfactory incision for operations on the gall-bladder and biliary passages which has been modified by various surgeons. A longitudinal incision is made through the upper rectus muscle extending obliquely along the costal margin, about an inch and a half from it and up toward the ensiform cartilage. The longitudinal part of the incision may be carried down to any desired length permitting careful abdominal exploration. In this respect its value in operations on the biliary tract is very marked, as an appendix may be removed or any necessary operation may be performed on the pyloric end of the stomach or duodenum. The incision made on the left side is equally advantageous in gaining access to the spleen. In working in the biliary region the longitudinal part of the incision is best made in the inner half of the rectus muscle, for splenectomy it is best made in the outer half. If the incision across the rectus muscle is kept an inch or more from the costal margin, this little flap, when caught with a catspaw, makes an excellent retractor.

Adhesions.—In most cases in which splenectomy is necessary, the spleen is enlarged and adherent to the parietal peritoneum and diaphragm especially over the upper pole. These adhesions differ greatly in their vascularity, being occasionally purely vascular, composed of a small artery and one or more varicose veins. Since these vessels cannot be seen and controlled until the spleen is loosened from its bed and drawn down, it is usually best to separate them with the fingers as close to the spleen as possible, trusting the control of any hemorrhage to a large gauze pack until the spleen can be delivered and removed (Fig. 1).

At times the spleen is firmly fixed in position by adhesions so strong they must be divided by a cutting instrument. By making an opening in the adhesions close to the splenic capsule and loosening the spleen as

* Read before the American Surgical Association, June 11, 1915.

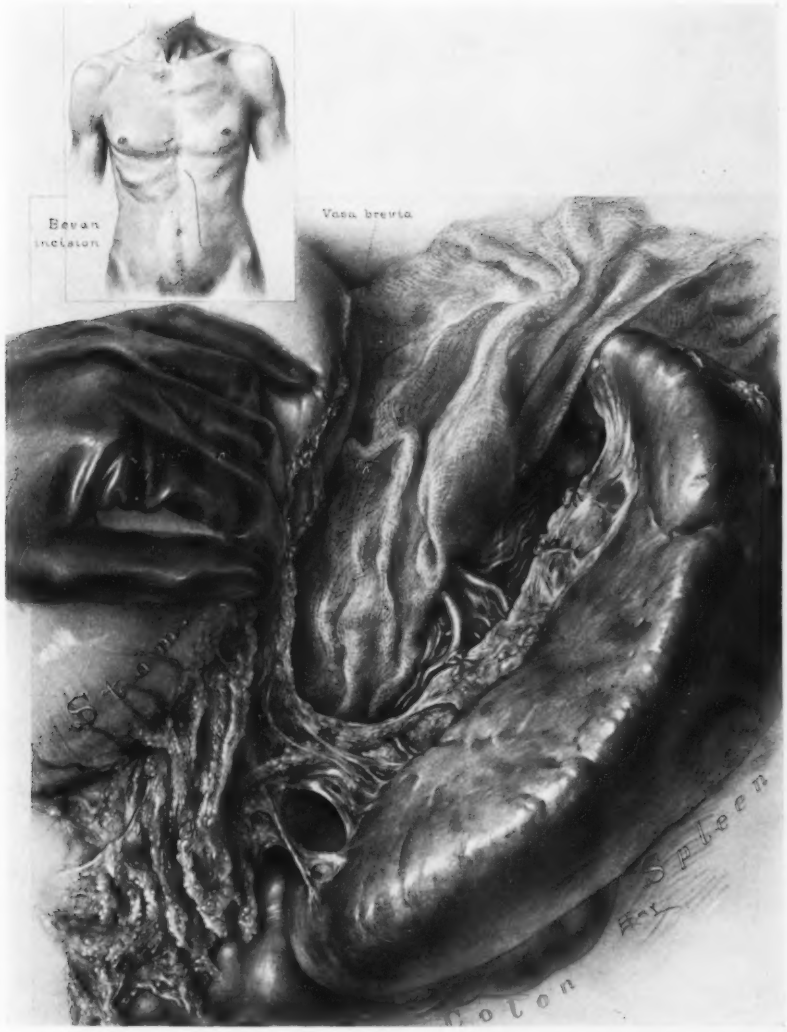

FIG. 1.—The Bevan incision for splenectomy, shown in upper figure. Lower figure—method of using gauze pack for temporary hæmostasis to control bleeding of separated adhesions.

FIG. 2.—Closure of splenic space by snaking catgut suture, to control oozing of blood from deep-seated areas.

far as possible by a combination of enucleation and division, a very adherent spleen may safely be removed.

A subscapular splenectomy, in the sense one speaks of a subscapular nephrectomy, is not possible. The capsule of the spleen is closely associated with the splenic pulp which is lacerated in the attempt to remove it from within the capsule, causing great loss of blood. With a little care, however, the spleen can be separated immediately at the capsule, leaving the attachments in a condition so there will be comparatively little bleeding. In this way the spleen can be quickly delivered and the pedicle temporarily controlled by fingers or an elastic rubber-covered pedicle clamp. The main thing to be accomplished is to leave the separated attachments in such condition that a gauze tampon will temporarily prevent bleeding. In two cases in my earlier experience the spleen was so firmly fixed with vascular adhesions, I did not deem it wise to undertake splenectomy.

Separation of the Splenic Ligaments.—Much may be learned concerning the normal relations of the spleen by operative work on the cadaver. The most serious vascular attachments are the vasa brevia in the gastrosplenic ligament which pass to the stomach. However, the bulk of these attachments can be delivered with the spleen, since the stomach can be drawn from the abdomen to a very considerable extent before separating the gastrosplenic ligament. Unfortunately, in a large adherent spleen there may be vascular connections in the deeper portion of the gastrosplenic ligament which pass inward and backward to anastomose with vessels along the spine and the crux of the diaphragm. Since these must be separated before the spleen can be eviscerated, early careful adjustment of an adequate gauze tampon, for temporary control of hemorrhage, may be essential. The lienorenal ligament has no great vascularity and can be readily divided. After the delivery of the spleen, the remainder of the gastrosplenic ligament and a leash of vessels passing to the inferior border of the spleen which connect it with the splenic flexure of the colon are tied in sections. This completes the peritoneal and omental attachments about the hilum, and, by dividing a few adhesions here and there, the spleen can be lifted up so that the vascular pedicle lies completely exposed for at least two inches.

Pancreas.—The splenic pedicle should be searched for the tail of the pancreas which, if present, will lie in the pancreatic notch of the spleen, behind the hilum. It can usually be readily separated, a few ligatures applied to bleeding points, and then dropped back into the abdomen. In three splenectomies, I [2] tied off a portion of the tail of the

pancreas with the splenic pedicle, in one case removing as much as an inch and a half, without any harm resulting. The spleen was bleeding so freely from lacerations that time could not be spared for separation. In the third case, in which the splenic vessels were atheromatous and would not hold a ligature, I tied the splenic vessels together with the body of the pancreas about three and one-half inches from its tip with two ligatures of catgut, three-fourths of an inch apart. The patient recovered without serious symptoms.

The pancreas has five independent sources of blood supply which protect its circulation. The pancreatic ducts have been shown clinically and experimentally to have great powers of regeneration. Fat necrosis as the result of escaping pancreatic secretion from injury to the pancreas in this situation, apparently is not to be greatly feared, probably because its secretions are not activated by duodenal secretion.

Vascular Pedicle.—In the average case, the vascular pedicle can be so thoroughly cleared that it may be easily ligated in sections. The artery should be tied first, but all vessels should be tied before any portion of the pedicle is cut. In spite of this precaution the spleen sometimes tears from the pedicle before it can be ligated. This accident happened in one of my cases—a fleshy patient. The spleen had a short pedicle which retracted deeply, but I was able to grasp the vessels in my fingers and hold them until forceps could be applied. In this type of case it is better to grasp the entire pedicle with elastic rubber-covered clamps [3] which will temporarily compress without damage any attached viscus, such as the wall of the stomach, until the splenic vessels can safely be controlled. In two instances I have injured the stomach because of its close attachment to the splenic pedicle, in one case ligating a portion of the wall of the stomach in the pedicle. Fortunately there was no escape of gastric contents and I was able to repair the damage. The patient recovered. In the second case I was less fortunate. There were large varicose veins in the gastrosplenic ligament and, in making a thorough exposure of the pedicle, one of the veins in the wall of the stomach was torn. Unfortunately, tooth-forceps were used to grasp the vessel and the fragile gastric wall was lacerated. There was an escape of gastric contents into the bed from which the spleen had been enucleated and the patient died a few days later from sepsis.

When the vascular pedicle has been carefully exposed but is too short for accurate ligation of the vessels, the two-forceps method will be found very satisfactory. In this procedure, two forceps are placed three-fourths of an inch apart on the pedicle and the spleen cut away

without regard to back bleeding. A catgut ligature is thrown around the pedicle, below the proximal forcep, which is then loosened and the ligature tied in the compressed area, while the distal pair of forceps steadies the pedicle and prevents retraction. A second ligature makes the pedicle secure.

There are undoubtedly some cases in which splenectomy is indicated but in which the condition of the patient or the attachments of the spleen make the operation inadvisable.

Two years ago I [3] suggested the possibility of ligating part of the vessels, believing that it would have an effect comparable to the ligation of the thyroid vessels in hyperthyroidism. I have not had an opportunity to carry out this suggestion and am not at all sure that it could be done with any degree of accuracy unless the delivery of the spleen were accomplished and in that event splenectomy would be equally easy and more effectual.

John Gerster [4] has suggested ligation of the splenic artery at the cœliac axis as a preliminary step in splenectomy, or in some cases as a method of producing atrophy of the spleen when it would not be practicable to remove it. He has mentioned the ease with which the cœliac axis can be reached through the gastrohepatic omentum. The splenic artery certainly could be conveniently tied at the cœliac axis, or just where it lies at the superior border of the pancreas.

Experimental ligation of the splenic artery demonstrates that the normal spleen will not become necrotic, but that it will undergo atrophy. The blood supply from the splenic artery to the pancreas and stomach which would be cut off by ligation is not important and would be well taken care of from the numerous anastomotic branches of other sources.

Closure of the Splenic Space.—This procedure is exceedingly important. Compression with the large temporary tampon will enable the smaller vessels to become sealed in a few minutes, but in the deeper recesses of the wound, there will probably be vessels requiring other treatment. With catgut on a small curved needle, the raw space, beginning at the tied splenic vessels, is closed as well as possible. The margin of the lienorenal ligament, on the outer side, is sufficiently firm to hold a suture, but on the inner side such bits of tissue must be caught here and there, as can be done safely until the bleeding vessels are compressed. The last sutures come well down on the diaphragm and had best be applied during cardiac diastole and during expiration. In some cases the splenic space will be dry when the tampon is removed and suturing is not necessary. To be able to leave the wound dry is a great satisfaction and well worth the little extra time taken to accomplish

it. One of my patients died of so-called secondary shock, due to failure to control hemorrhage at a deep point, and in two of my earlier cases, before I understood the value of the snaking catgut suture, I was compelled to leave a large tampon to control the oozing (Fig. 2).

Drainage is not needed unless there has been injury to some viscus. The after care is quite the same as that following any abdominal operation.

Mortality of Splenectomy.—The mortality of splenectomy depends more on the type of case accepted for operation than on the technical difficulties of the operation itself. If the patient is in good general condition, a small, movable spleen can be removed with a death rate so low as to be almost accidental. If the spleen is enlarged but has considerable latitude of motion, splenectomy may be performed with almost no mortality beyond the possible accidents of a serious operation. But if the spleen is enlarged and adherent and the patient is suffering from a high grade of anæmia with myocardial and renal changes, marked by œdema of the lower extremities, or is suffering from ascites, jaundice, high temperature, etc., the mortality will necessarily be high. Even under these conditions, surprisingly few patients die directly as the result of the operation. In 14 of our patients œdema of the lower extremities was marked. Seventeen had ascites with coincident myocardial and renal changes, 7 were jaundiced, and 5 were suffering from high temperature at the time of the operation. There were many combinations of these conditions, all in connection with high grades of anæmia, yet there were but 5 deaths in the hospital from all causes, in the 58 cases operated on. As shown by the post-mortem, 2 of the 5 deaths were from preventable causes (hemorrhage and sepsis). In conclusion, I desire to express my early indebtedness to J. Collins Warren [5] for his splendid paper, " Surgery of the Spleen," stimulating interest in the subject.

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CAVERNOUS ANGIOMA OF THE SPLEEN*

By Charles N. Dowd, M.D.
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The surgery of the spleen has been developed largely in the effort to modify certain complex diseases in which splenic inflammation or splenic enlargement is believed to be a factor; hence the great majority of splenectomies in recent years have been done for splenic anæmia.

There is, however, a very distinct literature on splenic cysts, splenic angiomas and splenic sarcomas. The borders of these three divisions are not definite, for some splenic angiomas have ruptured so as to form blood cysts and have been described under that heading, and others have undergone such changes as to be classified under sarcomas.

Powers,[1] Huntington,[2] Johnston,[3] and Musser[4] made valuable contributions to the subject, 1906–1911.

In 1913, Fowler[5] published an exhaustive study of cysts of the spleen. He follows the generally accepted classification into dermoid, parasitic and non-parasitic cysts. He confines his study mainly to the non-parasitic variety, of which he analyzes 82 cases, all that he could find recorded either from autopsies or from surgical clinics. In this entire series, only 2 were regarded as due to angiomas. This indicates the extreme rarity of cysts due to angiomas.

If we look for records of non-cystic angiomas we still find them very uncommon. Only 10 such records have been found which could fairly be included in the accompanying table.

Case Report.—The patient who forms the basis of this report was operated upon several years ago. The report was not then published as it was hoped that other similar cases would be observed. The extreme rarity of the condition, however, makes this unlikely, and, hence, it is offered as one member in the group of papers on the surgery of the spleen, which has been arranged for this meeting.

The patient, a well-nourished woman of thirty-seven, was admitted to the General Memorial Hospital, March 27. Her family and personal history had been negative excepting that 4 years previously a tumor had been removed from her neck, apparently a thyroglossal cyst. She had borne three children.

For six months she had suffered from pain in the splenic region. During a period of a week, two months ago, she had

* Read before the American Surgical Association, June 9, 1915.

suffered from repeated attacks of vomiting and epigastric pain, no blood in vomitus or stools. Three weeks ago she had noticed a lump in splenic region which had steadily increased in size. On admission to the hospital it had reached the proportions shown in Fig. 1.

Its margin was round, its consistency firm and it moved with respiration. There was no clinical evidence of abnormality in other organs.

Operation (April 1).—The mass was found to be a greatly enlarged spleen which was removed. It was adherent to the surrounding tissues and contained about 3 pints of blood in the parenchyma of its upper end. The so-called blood cyst thus formed was ruptured in removing the organ. There was no lining membrane in the resulting cavity.

The appearance of the specimen after shrinkage and hardening is indicated in Fig. 2.

Microscopical examination was made by Dr. William C. Clarke of Columbia University. Sections were examined from various parts of the organ. The spleen tissue had been practically replaced by a cavernous angioma.

Pathological Report (by Dr. Wm. C. Clarke).—Spleen measures 20 × 12 × 7 cm. In the larger end there is a blood distended cavity measuring 10 cm. in diameter. This produces a bulging rounded mass that projects evenly at the upper end of the spleen. The spleen surface is slightly lobulated and wrinkled throughout. There are two notches on the border. In the cut surface there are seen many hemorrhages in the splenic pulp. Adjacent to the larger cyst there is a single large hemorrhagic area 4 cm. in diameter. Microscopical examination of the spleen shows there are very many blood spaces of large size through the specimen. Between the large vessels are countless small ones. In the stroma there are free red blood-cells, showing that there have been blood extravasations. The stroma itself is scanty between many of the vessels and elsewhere it is exceedingly dense and cellular. In none of the sections examined is it possible to find any true splenic tissue intact; at points there are small aggregations of round cells suggesting lymphoid tissue.

To conclude, the bulk of the spleen is made up of blood-vessels and stroma to which is added extravasated blood.

Diagnosis: "Cavernous angioma of the spleen."

Figs. 3 and 4 indicate the appearance of the microscopical specimens.

At the operation many small, dark, cyst-like spots were noticed on the under surface of the liver; they were about ¼ inch in diameter, dark blue in color and appeared to contain small amounts of fluid. They were not elevated above the surface of the liver.

The subsequent history of the patient is most noteworthy and shows the sad possibilities of this type of tumor.

Her immediate recovery from the operation was satisfactory,

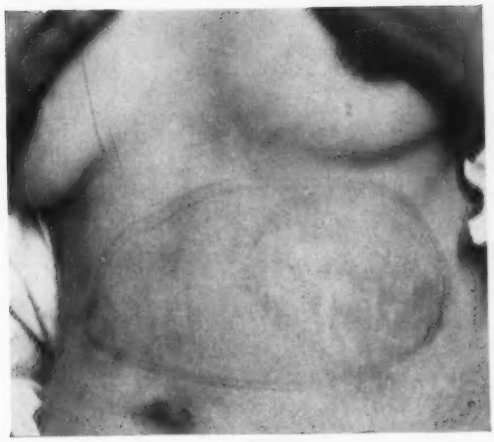

FIG. 1.—Showing outline of tumor as palpated through abdominal wall.

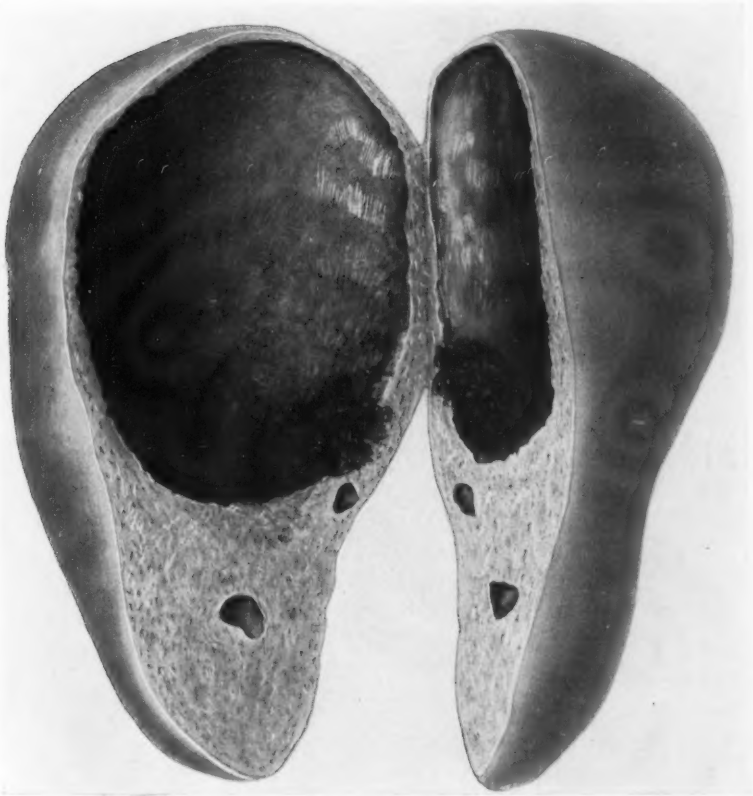

FIG. 2.—Drawing of spleen after shrinking and hardening. The splenic tissue was almost entirely replaced by cavernous angioma.

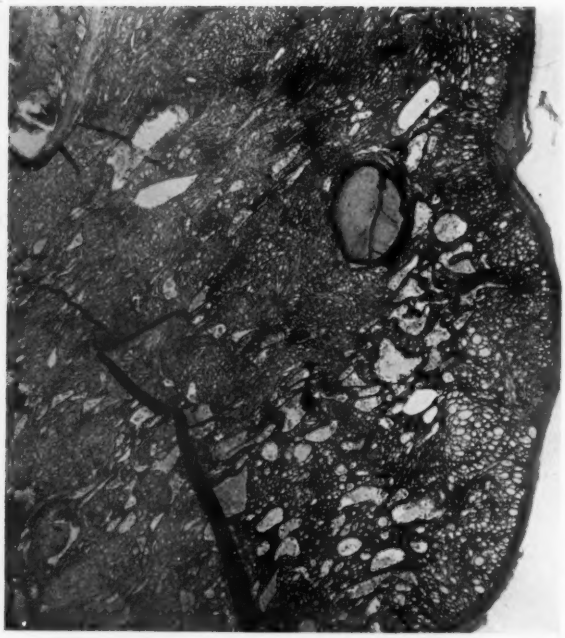

FIG. 3.—Microphotograph of cavernous angioma of spleen (low power).

FIG. 4.—Microphotograph of cavernous angioma of spleen (high power).

and on the twelfth day she was permitted to sit up. On the evening of the thirteenth day she had an attack of pain in the epigastrium and right hypochondrium and felt faint. The liver was enlarged and over it there was fremitus on respiration. It was believed that she had suffered a liver hemorrhage similar to that which had previously occurred in the spleen. She was kept in bed, horse serum was injected and she improved steadily for about a week, when the symptoms were repeated; and they came on again two weeks later. By May, her condition had become alarming: her pallor was extreme, she had moderate jaundice, and was very weak. Her red blood-corpuscles numbered only 699,200 per cubic millimetre and her hæmoglobin was only 25 per cent. of the normal. Transfusion was done and the hæmoglobin percentage raised to 40 per cent. This was followed by improvement, but by May 20, her people were discouraged and took her home where she died during the following month.

Before she left the hospital, there were signs of fluid in the lower part of the right side of the chest and bloody fluid was obtained by aspiration. The liver also showed much enlargement. It could be felt within one inch of the umbilicus. Ecchymotic discoloration also appeared about the site of the incision.

The following 15 blood examinations are recorded by members of the house staff, April 2 to May 20.

	Hæmoglobin percentage	Red blood-cells per cubic millimetre	White blood-cells per cubic millimetre	Polymorphonuclears and transitionals	Eosinophiles	Basophiles	Large lymphocytes	Small lymphocytes
April 2	70	4,448,000	30,600	88.3	5	6	3.7	1.5
April 3	70	.....	28,000	88	0	0	7	5
April 4	70	4,960,000	17,600	87	0	0	9	4
April 5	70	4,572,000	9,200	74	3	0	7	16
April 6	70	4,375,000	10,200	73	2	0	6	19
April 7	65	3,325,000	14,130	73	1	0	6	20
April 10	60	2,756,000	14,180	76	1	0	5	18
April 14	70	3,280,000	13,500	..	..	..	..	..
April 21	55	3,232,000	17,860	83	..	2	7	11
April 28	45	1,136,000	25,000	91	0	0	8	1
May 6	25	699,200	22,230	91	0	0	2	7
May 10	40	.....	.....	..	..	..	..	..
May 12	40	1,904,000	22,800	86	0	0	5	9
May 13	35	.....	.....	..	..	..	..	..
May 20	35	864,000	23,600	88	0	0	2	10

It is noticed that her anæmia became progressively worse and that she had a decided leucocytosis.

The main interest in this record centres in the growth which led to these overwhelming symptoms. Cavernous angiomas of the spleen with metastasis in the liver are very uncommon,

Jores,[6] in describing such a case in 1908, states that he is able to find records of only two other cases, those of Langhans and Theile.

In searching the literature, we have included in the accompanying table those cases which seem to bear directly on the subject. Some of the autopsy cases, however, showed very slight lesions. It is possible that under different headings records of other important cases exist; but this table is the result of many hours of search in the library of the Academy of Medicine by Dr. Charles E. Farr, and two weeks of continuous work there by Mr. Charles W. Lester.

The case of Langhans,[7] which was recorded in 1875 and which has been very extensively quoted through the intervening years, is almost the counterpart of the one here recorded. A robust acrobat aged thirty had a sudden pain in the splenic region and developed a pulsating angioma which involved nine-tenths of the splenic tissue and reached a size of $23 \times 15 \times 10.5$ centimetres. This was accompanied by metastasis of a similar nature in the liver which reached 3 or 4 times its normal size. He died after 4¼ months from exhaustion and suffocation.

Jores' case was also similar, a woman of forty-five who had a cavernous angioma of the spleen with liver metastasis. Death after 11 months from dropsy and cardiac weakness.

In Homan's case, it was believed that the omentum was also involved.

In Ernst's case, a child of 1¼ years, the liver was more involved in the angioma than the spleen, and there were 85 angiomatous spots in the skin.

In Theile's case the liver, stomach and lungs were involved.

Thus we see that in 6 of the 13 cases the spleen was not the only organ involved in the angiomatous growth.

Three of the remaining cases (Martin, v. Benkendorf and Anzilotti) recovered from their splenectomies and it is uncertain whether they had involvement of other organs.

The other 4 cases (Albrecht, Theile and Lubarsch) were reported from autopsies. The angiomas were small, no history of symptoms is given and there is no mention of angioma in other organs in 3 of the cases; the 4th died from perforation of the gall-bladder. They are included in the tables as minor grades of spleen angioma.

Histogenesis.—In connection with the published reports much has been written about the histogenesis of these growths. If we follow Moschcowitz,[8] who made an analogous study of cysts of the liver, we

TABULATION OF CASES WITH CAVERNOUS ANGIOMA OF THE SPLEEN. Prepared by Chas. W. Lester

No.	Observer	Recorded	Sex	Age	Duration	Symptoms	Operation	Result	Pathology	Involvement of other organs
1	Langhans.....	Virchow's Archiv, Bd. 75, p. 273	M	30	2½ mo...	Sudden pain, left side, region of ninth and tenth thoracic vertebræ. Swelling in left hypochondrium and epigastrium. Tumor evident on palpation. Pulsation and murmur	None.....	Tumor grew. Patient died two months after admission	Spleen enormously enlarged. 23×15×10.5 cm. Adhesions to diaphragm. Reddish-brown color. Cross-section—narrow periphery 1–5 cm. thick. Remainder cavernous with clots. Tissue of periphery somewhat like normal; no trabeculæ or follicles. Cavernous part tough, coarse-grained substance extending along walls and into cavern	Liver involved. Enlarged 3–4 times, 30×30×18 cm. Soft, tough, contained numerous red-dish-yellow knots. Cross-section showed substance to be filled with such knots—some containing clots. Knots measure 1–2 cm. in diameter.
2	Martin.....	Revue de Gyn. et de Chirurgie Abd., 1909, p. 67	F	..	Not reported	Pain in left hypochondrium. Loss of weight. Constipation. Tumor felt, supposed to be in spleen	Paramedian laparotomy and splenectomy	Cured. Discharged 2 months after admission	*Spleen:* Surface studded with violet-gray spots. Smallest punctiform—largest size 2 fr. piece. Cross-section showed spongy, compact and intermediate areas. Structure: compact area normal. Spongy, cavernous—mixture of Malpighian corpuscles and pulp. Trabeculæ of dense connective tissue. Microscopically: compact: slight connective tissue thickening, collections of red corpuscles. Intermediate: Venous sinuses enlarged. Central artery sclerotic. Lesion characterized by transition of splenic substance to cavernous. Filled with clots	None reported.
3	Homans.....	Annals of Surgery, 1897, vol. xxv, p. 732	F	22	1 year....	Swelling in abdomen. Very anæmic. Pulse 142. No pain. Tumor on right side which later disappeared, also row of small lumps extending across abdomen. Abdomen tapped 5 times for ascitic fluid	First, laparotomy with removal of tumor in great omentum, ovaries, supernumerary spleen and much fluid. Second, splenectomy	First, recovered and showed temporary improvement. But ascitic fluid returned. Second, died in 20 hours from shock	First operation: Small supernumerary spleen. Second: *Spleen.* Weight 415 gms.; size 15×11×4 cm. Numerous slightly elevated purplish areas on surface separated by splenic pulp. Areas were cavernous structures filled with blood and coagulated serum. Walls of thin connective tissue with endothelial lining. Diagnosis: *Cavernous angioma*	*Great omentum:* Tumor 10×3 cm., spongy, and fibrous fluid and clotted blood in cavities. Cavities pea-sized and smaller and communicating. Poor in nuclei; spindle-shaped when present. *Ovaries:* Numerous retention cysts, hemorrhagic contents. Diagnosis: Cavernous angioma. No autopsy.
4	Jores.....	Centr. f. Allg. Path. und Path. Anat., 1909, vol. 19, p. 662	F	45	11 months	Tumor in spleen noticed December, 1906; in liver, Spring, 1907. Died November, 1907	None.....	Died from dropsy and cardiac weakness	*Spleen:* Greatly enlarged, 31×15×16 cm.; weight 3.6 kg. Numerous protuberances on surface, slightly elevated. Little normal tissue visible on cross-section. Inside: structureless mass. Clot at one pole. Microscopically: Spleen necrotic, firm at border. Strands given off to interior containing red blood-corpuscles in their meshes. Structure that of *cavernous angioma*	Liver involved. Much enlarged, 38×35×15 cm.; weight 8.60 kg. Knots size of apple extending into interior and containing blood. Centre of knots showed diffuse hemorrhage, many blood-vessels at periphery. Knots were metastases.
5	Ernst.....	Verhand. d. deutschen Path. Gesellschaft, 1912, p. 232	M	1	Congenital	85 angiomatous spots on body. Died at age of 1 yr. 3 mo.	None.....	Died, asthmatic dyspnœa	*Spleen:* Involved secondarily. Angiomatous spots similar to those in liver but not so large or numerous	*Skin:* 85 angiomatous spots. *Liver:* filled with cherry-aised knots constructed from capillaries as in angioma simplex. Size 5–7 or 8 mm. in diameter.
6	Theile.....	Virch. Arch., Bd. 178, p. 296	M	56	6 months	Weakness in joints. Pressure and swelling in abdomen. No pain. Tumor felt in spleen. Blood examination: Hyperleucocytosis (1 : 350)	Splenectomy.....	Died, result of internal hemorrhage from small vessels day after operation	*Spleen:* Enlarged in all dimensions. Numerous round cavernous knots filled with blood under capsule. Knots of light and dark color. Light: elastic tissue enclosing spaces with very little blood. Dark: closely-packed blood-vessels containing blood and thrombus. Spindle-cell strands in tumor. Diagnosis: *Cavernous angioma*	Liver, stomach and lungs involved. *Liver:* spots similar to dark-colored tumors of spleen. Other spots of spindle-cell formation. *Lungs:* Have tumorous spots filled with blood similar to those in liver. *Stomach:* Small submucous sarcomatous and angiomatous tumors.
7	Albrecht.....	Zeitschrift für Heilkunde, 3, 1902, p. 97	M	65	.....	Autopsy report: Symptoms not given	None.....	.....	*Spleen:* Much enlarged. Normal shape. About 6 cavernous knots, bean- and pea-sized. Contain blood. Hyperplasia of pulp cells. Radiating fissures connecting arteries, blood spaces, caverns and veins. Malpighian corpuscles around cavernous blood spaces	None.
8	Theile.....	Virch. Arch., Bd. 178, p. 296	M	22	.....	Autopsy report by Lubarsch, S. No. 77, 1900	.....	.....	*Spleen:* Slightly enlarged, soft cherry-aised spots. Tumor sharply marked off. Numerous capillaries in periphery, endothelium swollen. Contain blood and thrombus. Spindle-cells between blood spaces: Centre cavernous, contains thrombus. Diagnosis: Obliterating angioma	None.
9	Theile.....	Virch. Arch., Bd. 178, p. 296	M	36	.....	Autopsy report by Lubarsch, S. 123, 1901	.....	.....	*Spleen:* Enlarged 14×7½×3 cm. Two firm reddish tumors, cherry-aised, at lower pole. Larger, similar to preceding case. Other composed of large and small freely-anastomosing blood spaces; mostly capillaries, some veins. Contain some thrombus. Diagnosis: Obliterating angioma	*None.* Gastric ulcer present.

IA OF THE SPLEEN. PREPARED BY CHAS. W. LESTER

	Result	Pathology	Involvement of other organs
...	Tumor grew. Patient died two months after admission	Spleen enormously enlarged. 23×15×10.5 cm. Adhesions to diaphragm. Reddish-brown color. Cross-section—narrow periphery 1–5 cm. thick. Remainder cavernous with clots. Tissue of periphery somewhat like normal; no trabeculæ or follicles. Cavernous part tough, coarse-grained substance extending along walls and into cavern	Liver involved. Enlarged 3–4 times, 30×30×18 cm. Soft, tough, contained numerous reddish-yellow knots. Cross-section showed substance to be filled with such knots—some containing clots. Knots measure 1–2 cm. in diameter.
pa- ple-	Cured. Discharged 2 months after admission	*Spleen:* Surface studded with violet-gray spots. Smallest punctiform—largest size 2 fr. piece. Cross-section showed spongy, compact and intermediate areas. Structure: compact area normal. Spongy, cavernous—mixture of Malpighian corpuscles and pulp. Trabeculæ of dense connective tissue. Microscopically: compact: slight connective tissue thickening, collections of red corpuscles. Intermediate: Venous sinuses enlarged. Central artery sclerotic. Lesion characterized by transition of splenic substance to cavernous. Filled with clots	None reported.
my l of reat ova- ner- and Sec- my	First, recovered and showed temporary improvement. But ascitic fluid returned. Second, died in 20 hours from shock	First operation: Small supernumerary spleen. Second: *Spleen.* Weight 415 gms.; size 15×11×4 cm. Numerous slightly elevated purplish areas on surface separated by splenic pulp. Areas were cavernous structures filled with blood and coagulated serum. Walls of thin connective tissue with endothelial lining. Diagnosis: *Cavernous angioma*	*Great omentum:* Tumor 10×3 cm., spongy, and fibrous fluid and clotted blood in cavities. Cavities pea-sized and smaller and communicating. Poor in nuclei; spindle-shaped when present. *Ovaries:* Numerous retention cysts, hemorrhagic contents. Diagnosis: Cavernous angioma. No autopsy.
...	Died from dropsy and cardiac weakness	*Spleen:* Greatly enlarged, 31×15×16 cm.; weight 3.6 kg. Numerous protuberances on surface, slightly elevated. Little normal tissue visible on cross-section. Inside: structureless mass. Clot at one pole. Microscopically: Spleen necrotic, firm at border. Strands given off to interior containing red blood-corpuscles in their meshes. Structure that of *cavernous angioma*	Liver involved. Much enlarged, 38×35×15 cm.; weight 8.60 kg. Knots size of apple extending into interior and containing blood. Centre of knots showed diffuse hemorrhage, many blood-vessels at periphery. Knots were metastases.
...	Died, asthmatic dyspnœa	*Spleen:* Involved secondarily. Angiomatous spots similar to those in liver but not so large or numerous	*Skin:* 85 angiomatous spots. *Liver:* filled with cherry-sized knots constructed from capillaries as in angioma simplex. Size 5–7 or 8 mm. in diameter.
...	Died, result of internal hemorrhage from small vessels day after operation	*Spleen:* Enlarged in all dimensions. Numerous round cavernous knots filled with blood under capsule. Knots of light and dark color. Light: elastic tissue enclosing spaces with very little blood. Dark: closely-packed blood-vessels containing blood and thrombus. Spindle-cell strands in tumor. Diagnosis: *Cavernous angioma*	Liver, stomach and lungs involved. *Liver:* spots similar to dark-colored tumors of spleen. Other spots of spindle-cell formation. *Lungs:* Have tumorous spots filled with blood similar to those in liver. *Stomach:* Small submucous sarcomatous and angiomatous tumors.
...	.....	*Spleen:* Much enlarged. Normal shape. About 6 cavernous knots, bean- and pea-sized. Contain blood. Hyperplasia of pulp cells. Radiating fissures connecting arteries, blood spaces, caverns and veins. Malpighian corpuscles around cavernous blood spaces	None.
...	.....	*Spleen:* Slightly enlarged, soft cherry-sized spots. Tumor sharply marked off. Numerous capillaries in periphery, endothelium swollen. Contain blood and thrombus. Spindle-cells between blood spaces: Centre cavernous, contains thrombus. Diagnosis: Obliterating angioma	None.
...	.....	*Spleen:* Enlarged 14×7⅓×3 cm. Two firm reddish tumors, cherry-sized, at lower pole. Larger, similar to preceding case. Other composed of large and small freely-anastomosing blood spaces; mostly capillaries, some veins. Contain some thrombus. Diagnosis: Obliterating angioma	*None.* Gastric ulcer present.

TABULATION OF CASES WITH CAVERNOUS ANGIOMA OF T

No.	Observer	Reported	Sex	Age	Duration	Symptoms	Operation	
10	Theile.....	Virch. Archiv, Bd. 178, p. 296	M	62	.....	Autopsy report by Lubarsch, S. 75, 1903	.....	.....
11	v. Benkendorf..	Virch. Archiv, Bd. 194, p. 500	M	53	2 years...	Abdominal swelling. Tumor felt	Splenectomy.....	Not r
12	Anzilotti.....	Lo Spermantale, Archivio de Biologia, Suppl. vol. 67, 1913, p. 161	F	38	14 months	Severe epigastric pains not related to meals often terminating in vomiting. Blood examination: reds 4,580,000, whites 4700, hæmoglobin 100 per cent., few platelets. Urine negative as to abnormalities. Leucocytosis followed operation lasting 45 days. Increase in platelets	Splenectomy.....	*Recov*
13	Dowd.....	.....	F	37	6 months	Pain in splenic region. Vomiting and epigastric pain. Lump noticed in splenic region, increasing in size	Splenectomy.....	Died later rhag of li

TABULATION OF CASES WITH CAVERNOUS ANGIOMA OF THE SPLEEN. PREPARED BY CHAS. W. LESTER.—*Continued*

Reported	Sex	Age	Duration	Symptoms	Operation	Result	Pathology	Involvement of other organs
Virch. Archiv, Bd. 178, p. 296	M	62	.....	Autopsy report by Lubarsch, S. 75, 1903	.....	.....	*Spleen:* Normal size. Greenish protuberances on surface. Firm dark red protuberance at upper pole, bean-sized. Smaller knot inside spleen. Several knots at lower pole. Tumors have same appearance as in preceding cases but richer in thrombus and spindle-cells. Diagnosis: Obliterating angioma	*None.* Cysts in kidney and œsophagus.
Virch. Archiv, Bd. 194, p. 300	M	53	2 years...	Abdominal swelling. Tumor felt	Splenectomy.....	Not reported.....	*Spleen:* Large cavernous area replacing three-fourths normal tissue. Sharply marked off from normal tissue. Venous capillaries enlarged, lengthened and walls thinned. Pulp between capillaries compressed and contains follicles and trabeculæ. Cavern contains lymphocytes, pulp cells, red blood-cells and colloidal substance	None.
Lo Spermantale, Archivio de Biologia, Suppl. vol. 67, 1913, p. 161	F	38	14 months	Severe epigastric pains not related to meals often terminating in vomiting. Blood examination: reds 4,580,000, whites 4700, hæmoglobin 100 per cent., few platelets. Urine negative as to abnormalities. Leucocytosis followed operation lasting 45 days. Increase in platelets	Splenectomy.....	*Recovered*.....	*Spleen:* Weight 1 kg. Several elevations on surface size of walnut, cyanotic color. In part cyst-like communicating structures lined with endothelium. Elastic fibres present. Were filled with fluid, blood clots, fibrin, or hyalin masses. Blood spaces dilated; pulp atrophic. Other localities showed transition into lymph tracts. Cross-section showed numerous angiomata giving cavernous structure. Malpighian corpuscles altered; trabeculæ thickened	None.
.....	F	37	6 months	Pain in splenic region. Vomiting and epigastric pain. Lump noticed in splenic region, increasing in size	Splenectomy.....	Died 2½ months later from hemorrhages in angioma of liver	*Spleen:* Measured 20×12×7 cm. Blood-distended cavity 10 cm. in diameter at larger end. Two notches on border. In cut surface many hemorrhages in splenic pulp. Adjacent to larger cyst is single hemorrhagic area 4 cm. in diameter. Microscopical: Many large vessels with small ones between. Free blood-cells in stroma. Stroma scanty. Diagnosis: Angioma of the spleen.	

find that studies in histogenesis have conformed to one of three theories: (1) inflammation; (2) tumor formation; (3) maldevelopment.

The inflammation theory represents the work of the older pathologists and was developed before bacterial infection was considered as important as we now believe. Virchow, for instance, wrote of intrauterine inflammation due to chemical irritation or mechanical obstruction. The painstaking description of the histological findings and the importance which is ascribed to blood-pressure and congestion and occlusion of vessels indicates a belief that some inflammatory change has been an element in the production of these growths. The writers, however, have been unable to give satisfactory evidence of such change.

As to the second, it is to be noticed that Jores found, in parts of his specimen, tissue resembling spindle-celled sarcoma, and hence used the term sarcomatous angioma.

Theile found in his case sarcomatous areas in the spleen, liver, lungs and stomach, and also used the terms angioma and sarcomatous angioma.

In most of the cases, however, there is no proof of sarcoma; the tumors are reported as angiomas and must be so regarded. They certainly have not shown the characteristics of malignant tumors.

If, however, we study the cases on the theory of maldevelopment, we have an explanation which at least is more plausible and more easily understood than either of the others. We are accustomed to observe congenital cutaneous and subcutaneous angiomas. Occasionally we find that they take on unexpected and even extensive growth; why they do so we do not know, but since the tissues themselves are abnormal, it does not seem very remarkable that their growth should be peculiar. We can better understand the existence of these angiomas on this basis than on any other which has been advanced.

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ABSCESS OF THE SPLEEN*

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A careful study of the literature, especially that of recent years, has conclusively shown that abscess of the spleen, usually regarded as more or less of a pathological curiosity, is of much more frequent occurrence than is ordinarily assumed. The occurrence of abscess of the spleen has been recognized from the earliest history of pathology and surgery, and reports of such cases come from all parts of the world. The condition, however, appears to be most frequently observed in the warmer climates, doubtless due to the more frequent occurrence of typhoid fever, malaria and dysentery. Abscess of the spleen has been known to follow typhoid fever, malaria, dysentery, relapsing fever, yellow fever, pyæmia, endocarditis, influenza, dengue, smallpox, diphtheria, anæmia, filariasis, and leukæmia. In short, it may follow any acute infectious disease, especially those associated with acute splenic tumor. Instances have also been reported in which spleen abscess has been secondary to appendicular abscess, salpingitis, puerperal fever, gangrenous chancre, carbuncle, and wounds of the external surface of the body. Any focus of infection may therefore be the portal of entry for the micro-organisms which may eventually produce abscess of the spleen. It has also been known to follow trauma as well as the twisting of the spleen pedicle in the so-called " wandering spleens." In a considerable number of instances, the portal of entry for the infecting micro-organisms has never been demonstrated and the symptoms referable to the spleen have dominated the entire picture. Abscess of the spleen always results from contiguous or metastatic infection, the latter being by far the more frequent. The instances in which spleen abscess has resulted from extension of infection by contiguity are comparatively few and have been associated for the most part with perforations of the stomach or subphrenic abscesses on the left side. It is also highly probable that a considerable number of cases reported as left subphrenic abscesses have been in reality abscesses of the spleen in which the involvement of the spleen has not been recognized. It certainly seems to be the fact that in the great majority of instances, intraperitoneal abscesses below the diaphragm on the left side are either abscesses of the spleen or have their origin in such abscesses. In many of the reported cases, no mention is made of the bacteriology of the abscess, but in a very con-

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siderable number the pus has been carefully studied and accurate reports made. In some instances, the abscesses have been shown to be sterile, while the bacteriology of those in which micro-organisms have been found has been very varied. Practically all the pyogenic bacteria, except the gonococci, have been described in connection with such abscesses, namely, bacillus typhosus, bacillus coli communis, streptococcus pyogenes, staphylococcus pyogenes aureus, pneumococcus, bacillus pyocyaneus and proteus mirabilis.

Considerable difference of opinion has existed as to the mode of development of the abscess in the spleen, many writers having regarded the abscesses as of embolic or thrombotic origin, originating in the infarcts, resulting from such emboli or thromboses. The frequent occurrence of such infarcts has been a strong argument in favor of this view, especially as such infarcts are known to occur in the interior of the spleen as well as upon the surface. Litten has especially emphasized the importance of thrombotic hemorrhagic spleen infarcts in the etiology of spleen abscess. Others are inclined to the view that abscess of the spleen may result from the activity of micro-organisms deposited in the spleen without the formation of infarcts. It would seem very probable that both views are correct, but it would appear that the greater number of spleen abscesses result from infected infarcts.

It very frequently happens that the cause of the enlargement of the spleen is not the direct cause of the abscess. Any condition which causes splenic enlargement may render it a *locus resistentiæ minoris* and, under such conditions, micro-organisms may gain a foothold which would otherwise cause no trouble. This is certainly the explanation of the occurrence of spleen abscess in association with or after malaria, leukæmia and other diseases associated with a chronic enlargement of the spleen.

Typhoid fever is undoubtedly the most common single cause of abscess of the spleen and the reason for this is quite evident, associated as it probably always is with an acute splenic tumor and occasionally with infarcts and hemorrhages in the spleen, as evidenced by Curschmann's findings of 25 cases of infarct and hemorrhage in 557 autopsies on individuals dead of typhoid fever. In the 557 typhoid autopsies reported by Curschmann, there were 4 cases of abscess of the spleen. Berg, of Leipsic, in an epidemic of 1626 cases of typhoid fever with 243 deaths and 228 autopsies, observed 4 cases of spleen abscess, while Vierhoff in Riga, in 1186 cases of typhoid with 112 deaths, saw 3 cases of spleen abscess. The severity of the infection does not appear to play a rôle in post-typhoid spleen abscess. In fact, Melchior states

that this complication is more frequently seen after the mild or moderately severe cases. There is often an afebrile period between the cessation of the typhoid fever and the onset of splenic symptoms. In many of the reported cases pure cultures of bacillus typhosus have been obtained from such spleen abscesses, while in other instances other pyogenic organisms have been found and in still other instances of post-typhoid spleen abscess the pus has been sterile.

Malaria probably comes next to typhoid fever as a factor of etiological importance in the causation of spleen abscess, but the views in regard to this are somewhat at variance, some authors claiming that spleen abscess in association with malaria is not especially infrequent, while others believe that it is very infrequent; as, for instance, Chowdhoory, who observed only 3 cases of abscess of the spleen in 30,000 cases of malaria in India. Italian writers have, however, reported a considerable number of cases in association with malaria, and its etiological importance is certainly established beyond question. Kernig, in 400 cases of relapsing fever in 1864–1866, observed 5 cases of abscess of the spleen; and Petrowski, in 359 cases of relapsing fever, saw 3 cases of spleen abscess. Ponfick, in a series of autopsies on cases dead of relapsing fever in one epidemic, found infarcts of the spleen in 40 per cent. of the cases.

Trauma is always of etiological importance both in normal spleens as well as those pathologically enlarged, and there are a considerable number of cases in the literature in which the direct relationship of trauma to spleen abscess has been conclusively shown.

Küttner has especially emphasized the importance of what he calls "sequestrating spleen abscess," a suppurative process, which is characterized by the presence in the pus of sequestra of spleen tissue. This condition, which occurs so often in abscess of the spleen, is but very rarely observed in abscess of the other abdominal organs and is regarded as of distinct diagnostic significance. The size of the sequestra may vary from minute bits to practically the entire spleen. Küttner in 1907 collected 116 cases of spleen abscess, 2 of which were in his own experience, and of this number 43, or 37 per cent., were of the sequestrating variety. The etiology of these 43 cases was grouped as follows:

1. Traumatic origin, 6 cases ..... 14 per cent.
2. Septic general infection, 11 cases ..... 25.28 per cent.
3. Post-typhoid spleen abscess, 6 cases ..... 13.95 per cent.
4. Post-malarial spleen abscess, 7 cases ..... 16.28 per cent.
5. Associated with twisted pedicle of wandering spleen, 2 cases.. 4.65 per cent.
6. Following perforation of the stomach, 3 cases ..... 6.97 per cent.
7. Cases of doubtful origin, 8 cases ..... 18.6 per cent.

Küttner conducted a series of experiments on dogs, and demonstrated that laceration of the spleen as well as infarcts may be the starting point of sequestrating spleen abscess. Küttner states that the presence of spleen tissue in a left-sided subphrenic abscess is proof positive of the existence of a sequestrating spleen abscess.

The symptoms of abscess of the spleen are in many cases not distinctive and can only be said to be suggestive. Enlargement of the spleen, as demonstrated by percussion or palpation or both, is practically always present, but this is of such frequent occurrence in many acute and chronic diseases without abscess that a great deal of importance cannot be attached to it. If the abscess is confined to the interior of the spleen no distinctive and almost no suggestive symptoms are present. It is only when the abscess reaches the capsule of the spleen and begins to cause disturbance in surrounding tissues that attention is especially directed to the splenic area. The local findings will differ according as the upper or lower pole of the spleen is more involved. If the abscess is in the lower pole, the spleen tumor will usually present below the costal margin and can be palpated. If the upper pole is involved, the diagnosis is more difficult and subphrenic abscess must be considered. One of the earliest and most constant symptoms that accompanies this stage of the disorder is pain, either spontaneous or elicited by pressure over the enlarged spleen. In many cases pain of this character is the only symptom complained of for a long time. Inflammatory involvement of the diaphragm and the pleura at the base of the left pleural cavity is one of the most important and suggestive symptoms of spleen abscess. This may lead to more or less restriction of movement of the left half of the diaphragm or an abnormally high position of the diaphragm on the left side, which can often be demonstrated by the fluoroscope or radiograph. A radiograph may give a very definite indication of a subphrenic or splenic abscess as in the case reported by the writer, and is of the greatest value in determining the diagnosis.

Pleurisy at the base of the left pleural cavity is a very common accompaniment of spleen abscess. It may be simply a dry friction or it may be a serous, serohemorrhagic or even purulent pleurisy, and in a considerable number of cases the condition has been regarded as one of pleurisy or empyema, and the origin of the process in the spleen has not been suspected until at operation or autopsy.

Fever of a remittent or intermittent type is a fairly constant symptom, although there are a number of cases in the literature in which there has not been any elevation of temperature above the normal.

Irregular chills have been noted in many cases. Leucocytosis of a rather pronounced character, from 20,000 to 50,000, has been frequently noted and especially emphasized by some writers as a diagnostic point of great importance, but in some cases there has not been any increase in the leucocytes, depending, of course, on many factors such as encapsulation of the abscess, reduced vital resistance, nature of the toxins, etc., so that this cannot be regarded as a constant sign. Nausea, vomiting and diarrhœa have been noted in not a few of the reported cases of spleen abscess. In a few instances œdema of the intercostal spaces over the splenic area has been noted. Exploratory aspiration is of the greatest importance in arriving at a diagnosis, and, while this practice has been decried by a few observers, the great majority unite in the belief that it is the most efficient method available for the determination of the diagnosis. It not only establishes the diagnosis, but gives a positive and definite indication for operation. Melchoir collected 17 cases of abscess of the spleen following typhoid fever, in all of which exploratory aspiration was practised without any untoward effects whatever, nor has it been possible to find in the literature any cases in which there is evidence that any bad effects have followed the employment of this procedure. It is also very evident that had it been used at an earlier stage of the disease, it would have been possible to establish the diagnosis in many cases at a time when treatment would have been more efficacious. Once the diagnosis is established, the only rational treatment is surgical, for, left to itself, abscess of the spleen usually results fatally, either from general sepsis or perforation into the peritoneal or pleural cavities, or some viscus. Spleen abscesses have been known to perforate into the stomach, intestine, pleural and peritoneal cavities, or even externally on the surface of the chest or abdomen, and in a few instances recovery has followed spontaneous evacuations of the abscess.

The surgical treatment is splenectomy or splenotomy, usually the latter. Splenectomy is to be employed only in such cases as are reasonably free from adhesions, or in which the organ can be removed without great difficulty or danger of spread of the infection. There are in the literature a number of successful cases of splenectomy for spleen abscess, but the great majority of the cases have been treated by splenotomy or drainage of the abscess cavity. The mode of operative procedure will depend upon the characteristics of the individual case, but will necessarily be through one of three routes: (1) the transpleural, (2) the abdominal, and (3) the retroperitoneal.

If the abscess involves the upper pole of the spleen, or presents the

characteristics of a subphrenic abscess, the transpleural route will be the most satisfactory. The ninth, tenth or eleventh rib, usually the tenth, is resected in the posterior axillary line, and in many instances adhesion of the pleura will have occurred in that locality, so that incision of the diaphragm and drainage of the abscess can be satisfactorily accomplished without infection of the pleural cavity. If the layers of the pleura are not adherent, suture of the diaphragmatic and parietal pleura should be performed and the abscess opened through the diaphragm either in a one-stage or two-stage operation as demanded by the conditions. Such a procedure does not, of course, allow of a splenectomy unless the entire spleen should have become sequestrated. The transpleural route is the shortest, but also the most difficult route to reach the spleen unless the pleural layers are adherent, when, of course, it is the ideal method.

The abdominal route is usually through an incision parallel to the twelfth rib, sometimes combined with resection of the twelfth rib. This gives free access to the spleen, especially if the abscess is located in the lower pole, or the spleen has been displaced downward. The danger from soiling of the peritoneum is comparatively slight and the opportunity for the establishment of drainage, or for splenectomy, if indicated, is excellent.

The retroperitoneal route has not been widely practised, but is strongly recommended by Propping. It consists in an incision between the anterior and midaxillary lines, extending from the tip of the twelfth rib along the lower margin of the eleventh rib. After severing the oblique muscles, one approaches the retroperitoneal or paranephritic tissues. The finger can be pushed along the under surface of the diaphragm towards its vault until the region of the abscess is reached and drainage established. If more room should be required, resection of the anterior part of the twelfth rib, or the anterior part of the eleventh rib can be done without much danger of opening the pleural cavity.

The prognosis of abscess of the spleen, recognized reasonably early and adequately treated surgically, is relatively good. Stucky places the mortality of reported cases at from 21 to 23 per cent. The best prognosis is afforded by the cases of spleen abscess following typhoid fever. In 22 such cases collected by Stucky, there were only 2 deaths, a mortality of 9 per cent. This is probably due to the fact that post-typhoid suppurations in general are relatively benign. The increased mortality in cases due to other causes is largely due to the nature or

continuance of the original disease, of which the spleen abscess is a complication.

The following case observed by the writer is reported in detail because it emphasizes many of the essential features of spleen abscess:

Mrs. M., twenty-seven years of age, had always been well and healthy, and had had three children. Some little time before the onset of the illness she was thought to have had an abortion performed, but no definite data as to this occurrence or its date were obtainable. On June 11, 1914, while in apparently good health, she was suddenly seized with a sharp pain in the left upper quadrant of the abdomen. The pain radiated to the back on the same side; the patient was nauseated, but did not vomit. The pain was not relieved by evacuation of the bowels and on the following day it became more severe and the abdomen slightly distended. She was up and about, and thought that she had some fever, although the temperature was not taken.

On June 13 a physician was called, the pain was still very severe and there was marked tenderness and muscle rigidity over the region of the left kidney. The spleen was not palpable and there was considerable abdominal distention, especially over the left upper quadrant. The urine was blood-tinged and contained numerous red blood-corpuscles. This, however, was not a catheterized specimen and the patient had been flowing slightly.

From June 14 to June 17, there was a marked decrease in the pain and there was only a trace of blood in the urine.

On June 18 the pain became much more severe, especially over the left lower quadrant of the abdomen and a fair amount of blood appeared in the urine. This condition continued until June 20 when the patient was brought to the Albany Hospital. There had not at any time been any cough or evidence of pulmonary disturbance. On admission to the hospital, the temperature was 101°, pulse 110, respiration 20. The patient looked sick and complained of sharp pain over the left upper abdominal quadrant, radiating to the back. The pain was not affected by respiratory movement of the chest. There was tenderness over the left upper abdominal region and some abdominal distention but nothing abnormal could be palpated and the pelvic organs appeared to be perfectly normal. The area of splenic dulness was somewhat increased and there was no muscle spasm in the left costovertebral angle, nor was there any other tenderness or evidence of disturbance in the abdomen. The liver was not increased in size. The heart and lungs were normal and there was no glandular enlargement or evidence of physical disturbance other than as noted. The urine showed a

trace of albumen and a few red blood-corpuscles. The leucocytes were 19,000.

On June 22, radiographs of the lower chest and abdomen were made, but were in every respect negative. During the succeeding days, the patient was greatly troubled with nausea and vomiting, with more or less intestinal distention and abdominal unrest.

On June 24, the ureters were catheterized and cultures from the urine thus obtained showed staphylococcus albus, which was probably a contamination. The urine contained a few red corpuscles, probably due to instrumentation, but no increase of leucocytes and no other abnormality. The Widals for typhoid and para A and para B were all negative. From June 20 to June 30 the patient's temperature was irregular in character and ranged from 98.6 to 102.4° and the chief complaint was of pain in the upper left abdominal quadrant, nausea, vomiting and some distention. The area of splenic dulness increased and the edge of the spleen could be felt at the costal margin and pressure over this area was painful. The leucocytes ranged from 20,000 to 24,000.

On July 1, the temperature fell to normal with a general improvement in all the symptoms and for six days the temperature remained normal, with practically a disappearance of all symptoms except some slight pain in the region of the enlarged spleen. The urine was normal except for a slight trace of albumen, and the leucocytes on July 3 were 12,400.

Everything seemed to be progressing most favorably. The patient's appetite had improved and she was planning to return to her home, when, on July 7, the temperature went up to 100° and on the day following to 102.6°. There was a marked increase of the pain in the region of the spleen and the nausea and tympanites returned. The only physical evidence of abnormality aside from the tympanites was the enlarged spleen and pain on pressure in this region. The leucocytes on July 9 had risen to 22,400. All of the Widals on July 11 were again negative. Blood cultures on July 13 were negative.

July 14, the patient for the first time complained of being chilly. The patient's temperature had assumed a remittent septic type and the spleen had become more enlarged and could be readily palpated two centimetres below the costal margin.

July 17, dulness in the midaxillary line extended upward to the ninth rib, but aside from the dulness and absence of breath sounds in that region, there was no evidence of any pleural or pulmonary disturbance. Exploratory aspiration was done in the

ninth interspace in the posterior axillary line and only blood obtained. The leucocytes were 22,400.

From July 17 to August 4 the patient had frequent slight chills and her temperature, which was of a remittent type, ranged from 98° to 104°. There was considerable nausea and vomiting with tympanites and the patient was evidently losing ground. Numerous Widals were done and on one or two occasions were reported as suspicious for typhoid. All of the signs pointed to the splenic region where the patient complained of all her pain.

August 2, exploratory aspiration was again done through the ninth interspace in the posterior axillary line, but was negative.

August 4, a radiograph was made, which showed an arching upward of the diaphragm on the left side posteriorly as far as the middle of the eighth interspace. Both pleural cavities were normal. Below the diaphragm there was an irregular area of shadow extending from the ninth to the eleventh ribs inclusive, posteriorly and to the outer side of the abdominal cavity corresponding to the position of the spleen. Over a part of this shadow was the shadow of a coil of intestine containing gas, probably the splenic flexure. Exploratory aspiration was again employed in the tenth interspace posteriorly into the area of shadow indicated by the radiograph and this time pus was located at a considerable depth. A portion of the eleventh rib was resected posteriorly by my assistant, Doctor Donhauser, during my absence from the city and a small abscess deeply seated below the diaphragm was opened. Cultures from the pus showed a pure culture of pneumococci. There were, however, absolutely no signs or symptoms of pleural or pulmonary involvement. Following this operation the patient's general condition seemed to improve and for a few days the temperature was not quite so high, but after a few days she began to lose ground again, had chills and profuse sweating, with nausea and tympanites.

August 20 another blood culture was made and reported as negative. Mixed vaccines were then employed and continued for some time without any appreciable effect. The drainage from the wound diminished.

August 24 another radiograph was made, which showed both pleural cavities normal and a much less distinct shadow where the abscess had been opened in the left side.

August 27, for the first time, the patient began to complain of pain in the liver region and the liver was found to be somewhat enlarged and rather sensitive.

August 28, for the first time, the patient coughed a little, but no evidence of any pleural or pulmonary disturbance could be found.

FIG. 1.—Showing arching upward of diaphragm on left side, with shadow of splenic abscess below diaphragm—indicated by arrow.

On August 29 it was felt that an opportunity for freer drainage of the left side was desirable and the writer resected a considerable area of the tenth rib as well as more of the eleventh rib and followed the track of the sinus through the diaphragm into the spleen, which was found to be riddled with abscesses, with some areas of sequestrated splenic tissue, the largest of which was the size of a walnut. These areas of tissue, examined at the Bender Laboratory, were reported as "acute splenitis." Very free drainage was thus established and profuse discharge occurred during the succeeding days. The patient's condition, however, grew steadily worse. She complained of much pain over the region of the liver and the liver became much enlarged with some icterus. She presented the appearance of a suppurative portal pyelophlebitis, which she was believed to have as a complication of the spleen abscess. Occasionally the patient would have attacks of coughing with some mucus, or mucopurulent, expectoration. She grew steadily weaker, the temperature ranging from 96.8° to 104.8°, until on September 20 she had a sudden attack of pulmonary œdema associated with the expectoration of a considerable quantity of mucopurulent material and died. An autopsy could not be obtained.

Unfortunately the original portal of entry for the micro-organisms in this case could not be positively demonstrated, but the fact that an abortion was thought to have been performed a short time before the onset of the disease would indicate that possibly the uterus was the portal of entry and that the case might be classified as a spleen abscess secondary to puerperal infection. The pronounced intestinal symptoms early in the disease as well as subsequently necessitated the consideration of the intestine as a possible portal of entry. There is also the possibility that the primary disturbance may have been an hæmatogenous infection of the left kidney, which soon cleared up. The enlargement of the spleen developed in the early stages of the disease and persisted, although somewhat reduced in size, during the afebrile period of six days when the patient appeared to be on the road to recovery. The recrudescence of fever was doubtless due to the splenic infection, which escaped detection from July 8 to August 4 in spite of the most careful examinations and repeated exploratory aspirations of the area of the splenic dulness. When finally the abscess was located by radiograph and aspiration, the infectious process had gone too far to be favorably influenced by surgery, in spite of the vigorous efforts made to provide free drainage. The final picture presented by the case was one of portal pyelophlebitis in all probability

secondary to the abscess of the spleen. It seems quite reasonable that had an exploratory laparotomy been done in the earlier stages of the disease and the splenic area carefully examined and properly treated, a more favorable outcome might have been had, but the acute splenic tumor so common in acute infectious processes hardly seemed a sufficient justification for such a procedure.

It is to be hoped, however, that the study of such cases as this will lead to the earlier exploration of the splenic region in cases which present such definite subjective and objective symptoms as those here related.

PAPILLOMAS OF THE GALL-BLADDER*

By Charles H. Mayo, M.D.
of Rochester, Minnesota

Few new operations on the gall-bladder have been developed recently. Very early in the surgery of gall-stones cholecystotomy, cholecystostomy and cholecystectomy were common procedures, some surgeons advocating one and some another.

Later, exploration of the ducts, especially in cases in which jaundice was or had been a factor, was practised by some surgeons who reported an unusually large percentage of cases of common duct disease, as primary instead of secondary surgical procedures, such examinations also disclosed pancreatitis of some form as an occasional complication. Pancreatitis had been considered a rare disease by those who did not explore and whose knowledge was derived from autopsy reports. Such explorations at the operating table led to the cure of a larger percentage of cases, many patients being saved time and dangers of a second operation. The same can be said of examinations of the appendix for associated disease at operations on the stomach and duodenum for ulcer.

In an early day surgeons were often chagrined in operating for gall-stones to find no evidence of stone, but an apparently healthy gall-bladder. In these cases general exploration was forced upon them and thus the advantage of always exploring, when not contra-indicated, became an accepted routine of abdominal operations. Cholecystitis associated with stone formation was commonly noted. Thick-walled gall-bladders without stones, but giving symptoms of cholecystitis, were next drained or removed. Stones were occasionally found in thin-walled and blue gall-bladders which, when free from adhesions, formerly had been considered free from disease. Some such gall-bladders, upon cholecystostomy, showed the peculiar markings of "strawberry" (Fig. 1) mucosa. It was then appreciated that a disease of the mucosa could exist in a gall-bladder which from its external appearance was apparently healthy. In cases in which well-marked symptoms of gall-bladder disease existed the gall-bladder was opened, examined and drained, or removed according to the personal judgment of the operator after he had proved to his satisfaction that the symptoms were not caused by other abdominal conditions. Such gall-bladders were described as "catarrhal," a term which always leads one to think of an excessive mucous secretion or of a mucosa with a diseased surface, but which really means inflammation at the base of the cells involved.

* Read before the American Surgical Association, June 10, 1915.

If an inflammation is from bacterial infection the lymphatics draining the diseased area are enlarged and soft in acute processes and harder in chronic processes from exerting their protective function against acute general involvement by absorption. Lymphatic glands are always located at the neck of an organ in movable tissues adjacent to the vascular supply. There are two or three glands on the cystic duct and several along the hepatic and common ducts; the latter drain the head of the pancreas and the duodenum. Inflammation of the pancreas, however, usually involves also the gall-bladder or ducts. Ulceration of the duodenum may cause swelling of these glands. If the symptoms of gall-bladder disease indicate exploration and upon examination there are no gall-stones and but little change in the appearance of the gall-bladder, these glands should be palpated. Given sufficient symptoms for surgical intervention, if these glands are swollen without other adequate cause as from diseased duodenum, pancreas or general abdominal infection, the gall-bladder should be removed whether or not stones are present. On the other hand, given such symptoms, if no gall-stones are found and if the glands are not swollen, then some other cause for the symptoms must be searched for, since the patient probably will not be relieved by an operation on the gall-bladder.

What causes inflammation of the gall-bladder? There are several theories. First, that of an ascending infection from the duodenum by way of the ducts; second, infection by way of the lymphatics; and third, infection by the portal route through the liver which fails to destroy the bacteria brought to it. The first theory, that is, ascending infection, has not been generally accepted. The second, that is lymph stasis, has been accepted with considerable reservation for some conditions. The third, that is, living bacteria in the bile which have passed through the liver, has been more generally accepted. The first and last theory, however, acknowledge that living bacteria in the bile penetrate a living healthy mucosa lining the gall-bladder which is made for, and should be able to, protect itself against such conditions. To believe this we must consider the surface of the mucosa as the vulnerable point, which is possible but less probable than that the attack is commonly in the unprotected rear, that it is by way of the blood stream.

The vascular route as suggested by Rosenow looks very plausible. We have long accepted the fact that the well-known infectious diseases have each a specific bacterium which causes, according to the type, a definite group of symptoms in lungs, intestines, skin, mucous membranes, tonsils or elsewhere. To Rosenow is the credit due for the theory that the bacteria which cause similar acute and chronic diseases,

FIG. 1.—132852. Strawberry gall-bladder.

FIG. 2.—A106500. Papillomata.

FIG. 3.—A78954. Papillomata and strawberry gall-bladder.

FIG. 4.—96944. Chronic cholecystitis, strawberry gall-bladder with papilloma.

such as cholecystitis, have the same definite function, and that when they enter the blood stream they search out locations with the same environment as that in which they originated. He has shown that changes in environment can change bacteria in appearance, and in the effects caused by them, and in their tendency to locate in vascular or mucous surfaces, or to cause inflammation of the joints. Such bacteria are cultured in a certain focus in the body and thence through the vascular system, producing a varying degree of infection in a gall-bladder, while bacteria cultivated from acute gall-bladder inflammation entering the vascular system may produce similar acute gall-bladder inflammation in another individual. In certain investigations, some of which were made at our Clinic, Rosenow has shown that bacteria cultivated from the tissues of the gall-bladder and those from the glands along the ducts showed similar growth; further, that such cultures of bacteria injected into dogs caused similar changes in their gall-bladders. Such a result occurred approximately in two-thirds of the experiments. Not alone, however, is the gall-bladder affected. Some experimental animals show associated rheumatism and some heart, kidney or other involvement due to bacterial changes from new environment.

Cholecystitis then is a disease of the gall-bladder caused by bacterial invasion of the wall of the structure. In this direct manner do we have changes in its circulation with œdema, infiltration, exudation, swelling of the lymphatic glands and local necrosis of the mucous membrane; for example, strawberry gall-bladder. This infiltration of the gall-bladder structure with cells and bacteria prevents the distention and contraction of the sac and causes pain. Thus may be caused qualitative food dyspepsia and symptoms of epigastric gas pressure.

Papillomas of the gall-bladder occur in the same manner, but instead of a primary destructive effect, there occurs locally a hyperplasia or overgrowth which later may become necrotic. That the disease is more common than is ordinarily supposed is indicated by the fact that it was found 107 times in 2538 cases of cholecystectomy made at our Clinic from January 1, 1907, to June 1, 1915. The glands above described were enlarged in these cases. The pathology of these cases has recently been studied by MacCarty and Irwin, who summarize the results of their observations as follows:

"The diseases of the gall-bladder have been classified as follows: 1. Acute catarrhal cholecystitis. 2. Chronic catarrhal cholecystitis. 3. Papillomatous catarrhal cholecystitis. 4. Malignant papillomatous cholecystitis. 5. Carcinomatous catarrhal cholecystitis. 6. Chronic cholecystitis. 7. Chronic cystic cholecystitis. 8. Purulent necrotic cholecystitis."

"Of these, groups 3 and 4 have been the subject of the present study. In all the cases in group 3 (Figs. 2–4), papillomatous catarrhal cholecystitis, the mucosa is intact. The papillomas vary from twice to five or six times the length of normal villi. They are usually pedunculated, frequently racemose and usually white or yellow. They appear in any portion of the organ, being confined neither to the neck nor the fundus. Upon microscopic section, they appear to be hypertrophic villi, the tissue elements of which present a hyperplastic condition. The connective tissue and glandular tissue are greatly increased, the latter being so distorted that sections cut the glands in many different planes. The epithelium of the glands is hypertrophic and occasionally hyperplastic and practically always completely covers the growth. In the stroma one often finds large round or oval cells which contain fat or some fatty substance, this condition probably being responsible for the yellowish gross appearance of the growths."

"In no case are there any early signs of carcinoma, although similar hypertrophic conditions of the villi have been seen in association with carcinomatous outgrowths of the gall-bladder. The condition occurs in acute catarrhal cholecystitis, chronic catarrhal cholecystitis, cystic catarrhal cholecystitis, carcinomatous catarrhal cholecystitis and purulent necrotic catarrhal cholecystitis. It occurs with and without the association of stones, and is more frequent in females than in males, probably due to the fact that more gall-bladders are removed from females.

"Papillomas are but an associate pathologic condition found in cholecystitis. One theory of origin is that they possibly originate in surface cracks through overdistention, caused by mucous obstruction and swelling of the mucosa incident to cholecystitis associated with the presence of bacteria or irritants from stagnation of gall-bladder contents. It is, however, not so plausible as Rosenow's theory of vascular-borne infection of the gall-bladder mucosa.

"Like papillomas in other portions of the body, those in the gall-bladder undergo an irregular or perverted epithelial hyperplasia which manifests itself in marked reduplication of the rows of epithelial cells. This condition constitutes malignant papillomatous cholecystitis. Differentiation between this condition and carcinomatous catarrhal cholecystitis must be made with reserve because it is possible that the one is but a stage of the other."

From the surgical standpoint, it is important to note that the papillomas of the gall-bladder are not cured by temporary drainage but that cholecystectomy should be performed.

A REPORT OF THE CASES OF GALL-STONE DISEASE OPERATED DURING THE YEAR 1914 *

By John B. Deaver, M.D.
of Philadelphia

In reviewing the case records of gall-stone disease operated in my clinic at the German Hospital during the year 1914, and in comparing the pathological findings at the operating table with the *subjective* symptoms presented by the patients, and the operative procedures with the ultimate relief afforded, my attention was drawn to a few salient points which are here presented in a more or less statistical form.

The cases presented number 159; 87 of which are classified as simple gall-bladder disease, including types of cholecystitis with or without stones; 20 cases of gall-bladder and common duct involvement; 52 cases of gall-bladder disease with secondary pancreatic involvement, and 7 re-operative cases.

The average age of patients at the time of operation was forty-four years; in simple gall-bladder disease forty-five years; and in those cases with involvement of the common duct, or of the liver and pancreas, forty-seven and forty-one years, respectively. The age of the pancreatic cases was lower at operation, owing to the greater severity of symptoms which drove these patients to seek operative relief at an earlier date.

The decade of life showing the greatest frequency in all cases was between forty and fifty years, averaging 36.8 per cent. in the uncomplicated cases, 40 per cent. in the common duct cases and 46.4 per cent. in the pancreatic cases. The next period of greatest frequency was between thirty and forty, averaging 24 per cent., 15 per cent. and 33 per cent. respectively. Simple gall-bladder disease shows a higher percentage below forty years than those with secondary involvement, and above fifty and below thirty the frequency diminishes rapidly, this trend being even more marked in the common duct cases. It is to be noted that though the incidence of frequency increases progressively up to the age of fifty, it does not correctly represent either the beginning of the acute process or the time of formation of the stones. Doubtless many start in early life and remain relatively dormant, except for a few vague premonitory symptoms which are diagnosed and

* Read by title before The American Surgical Association, June, 1915.

treated as gastritis, indigestion and dyspepsia. The many acute infectious diseases which occur during early adult life may start the process in the gall-bladder and, as middle age approaches with its more sedentary habits and resultant stagnation of bile flow, result in definite gall-bladder lesions.

Gall-bladder disease is more frequent in women than in men; in the simple cases 85.1 per cent. were females, or, as Schroeder has shown, five times more frequent; in the other two groups 60 and 70 per cent. respectively were females with a diminishing ratio of 2.2 to 1.

The largest number of males is found in the group characterized by pancreatic involvement, a fact which agrees with previous studies of pancreatitis by Pfeiffer and myself, which showed the greater liability of males to pancreatic disease.

Stagnation of bile flow and infection, which are respectively the predisposing and exciting causes of biliary disease and stone formation, find their greatest opportunity in the female sex. The natural sedentary habits of the female, poor muscle tone, ptosis of the abdominal organs, especially the liver, causing kinking of the extrahepatic ducts and the many pelvic infections, account for the great frequency in this sex.

An analysis was made also of the female cases before and after forty-five, the accepted age of menopause. It is well known that common duct cholelithiasis is merely the result of the wandering of stones from the gall-bladder when they are forced through the cystic into the common duct. It is but natural, therefore, that common duct involvement, representing, as it does, a later stage of the same disease, should show a later age incidence as noted in this series; common duct cases were more numerous after the menopause. Uncomplicated gall-bladder disease, as well as that associated with pancreatitis, was most numerous before that period.

The duration of symptoms before operation was eleven months in all cases, but in simple gall-bladder disease and in the pancreatic cases the time intervening was over three years. In the common duct group 30 per cent. were of one to five months' duration.

The diagnosis of gall-bladder disease is not always a simple one, owing to the many structures in close proximity to it and the resultant complications which follow infection in this region, but the most consistent symptom has been a long-continued history of indigestion and flatulency with recurrent attacks of pain in the epigastrium and upper right abdominal quadrant. This pain is a constant symptom, not always of the sharp colicky character so typical of the movement of a

foreign body passing from a larger tube to a smaller one, but dull, constant or intermittent discomfort in the gall-bladder region. Of all the cases in this series 94 per cent. had pain which was most constant in the upper right abdominal quadrant; in the simple cases 64 per cent. had pain in this region, but the majority of the pancreatic cases had pain primarily in the epigastrium.

Sharp colicky pain may also be due to infection of the regional peritoneum with subsequent adhesions. Sixty-one per cent. of the simple and pancreatic cases had this character of pain and in these cases at operation many pericholecystic adhesions were found.

Riedel has laid stress on the fact that sharp colicky pain in gall-stone disease is not always due to stone, and gives the following causes of colicky pain in gall-stone disease.

1. Adhesions of gall-bladder without stone.

2. Adhesions with large stones in the gall-bladder and the cystic duct patent.

3. An inflamed distended gall-bladder containing stones with an occluded cystic duct or a stone in the neck of the gall-bladder.

4. Inflammation of the common duct.

5. Transit of a stone through the extrahepatic ducts.

To this should be added the biliary obstruction which sometimes accompanies exacerbations of pancreatic inflammation.

Referred pain was a fairly constant symptom, found most often in the right shoulder and right costal border. Some cases had referred pain to the right iliac fossa, but in these cases a chronically diseased appendix was found. Occasionally pain will be referred to the left hypochondrium or back, and in these cases secondary adhesions of the duodenum or stomach are commonly found.

The duration of pain was analogous to the duration of symptoms in most cases, extending over a period of three years in all cases.

The period intervening since the last attack was short, being one week in 30 per cent. of cases.

Tenderness and rigidity were also present, especially during or shortly after an attack of acute pain, but even in the more chronic cases as a rule deep palpation under the costal border elicited some tenderness and resistance to the palpating hand.

Vomiting after meals was most often present in simple gall-bladders, but indigestion, flatulency and nausea were found most frequently in common duct cases. Constipation was a variable symptom found in most cases but most common in pancreatic lesions.

The fact that jaundice is not always due to demonstrable obstruction

of the ducts was shown clearly in these cases. Jaundice was found in all groups. In simple gall-bladder disease it was present in 41 per cent., in common duct cases in 55 per cent., and in pancreatic involvement in 38 per cent. There are many causes of jaundice other than stone obstruction. In general it may be said that the chief cause of jaundice other than actual mechanical obstruction, which is surgically removable, is infection which may act either on the extrahepatic ducts, causing swelling, and in that way occluding the ducts of discharge, or the infection may ascend into the finer radicles of the bile ducts, causing what has been termed a cholangeitis, and in this manner give rise to intrahepatic obstruction and the discharge of bile into the lymph and blood streams.

Not much help is derived from laboratory and X-ray findings. That the X-ray can show gall-stones in a percentage of cases there is no doubt, but that this is fortunate I am not prepared to say. Too much confidence placed in X-ray diagnosis will influence the patient, I fear, and perhaps the doctor as well, to procrastinate. In the absence of positive findings this would be most unfortunate, as we know that gall-stone disease advances and does harm through infection and not merely as the result of gall-stones themselves.

The blood showed slight diminution of hæmoglobin and erythrocytes in common duct cases, and the leucocytes on an average were fairly constant. Not much reliance can be placed in coagulation time, as the present methods of determining it are very inadequate and unscientific. In simple gall-bladder cases the average was 4.6 minutes. The longest in the pancreatic cases was 14 minutes.

From the examinations of the stools and test-meals we derived very little benefit in making a diagnosis. Most stools showed bile and a majority showed occult blood to the benzidin test, while 9 cases were positive to the guaiac test for occult blood. The test-meals for free and total hydrochloric acid averaged 16 free HCl and 40 total acidity.

. *Operations and Operative Findings.*—The mortality in the entire series was 6.3 per cent., being distributed as follows: in uncomplicated gall-bladder disease 4.5 per cent., in common duct cases 5 per cent., and in gall-bladder disease plus pancreatic involvement 9 per cent. The total number of deaths was 10. In 2 cases carcinoma was present, involving the gall-bladder in one case and the pancreas in the other. Two perished from uncontrollable hemorrhage, the sequel of chronic cholæmia which I have found no means to control. Two cases died of cardiac insufficiency. One died of obstruction two months after operation, one of peritonitis, one of pneumonia and another died on the table

of respiratory failure following the use of intraspinal stovaine. Over half of these deaths can justly be attributed to delay as much as to the operative procedure. Carcinoma, it seems probable, is in some way associated with the chronic irritation of long-existing infective processes. Myocarditis is, as Babcock has so well pointed out, a direct result of the toxæmia of upper abdominal infection. Chronic cholæmia to the degree of robbing the blood of its coagulation properties is an arraignment of the management of the case.

The type of operation was determined by the pathology found. In general the indications for cholecystectomy were extended as compared with my former practice. Thickened, functionless gall-bladders and those showing a condition of empyema, mucocele, or imbedded stones were sacrificed without hesitation. In addition to these a large group of obviously infected gall-bladders, with or without stones, but complicated by pancreatitis or peripancreatic lymphangitis, were treated by cholecystectomy. The reason for this is partly to be found in the demonstration by Rosenow that the gall-bladder wall in these cases harbors virulent bacteria, partly in the fact that the extension of the inflammation which was being transmitted to neighboring structures constituted too gross a menace to assume risk of further trouble, and finally in the desire to avoid a percentage of recurrences after simple drainage of the gall-bladder, which it has been my lot to observe.

Almost without exception when the gall-bladder was removed a choledochostomy was made and drainage accomplished by means of the T-tube. Drainage I regard as the most essential part of operations upon the biliary tract. It should be prolonged rather than short. I have under observation a case referred by my colleague, Dr. Riesman, in which the patient has been carrying a T-tube in the common duct for over two years. She refuses to allow it to be removed, having experienced on two former occasions a recurrence of symptoms after removal of the tube. This is exceptional, but it shows how well the tube is tolerated and how efficacious it is in relieving back pressure upon the liver in cases of blockage by enlarged pancreas, strictured duct or other cause of obstruction.

It is not easy in borderline cases to determine whether to remove the gall-bladder or leave it. When pronounced disease is present I feel that the best ultimate result will be obtained by removal if the case is in skilled hands. The operative mortality should not be materially increased over that of cholecystostomy in the same group of cases.

A cholecystectomy alone or associated with other operations, as

appendectomy, choledochostomy, gastrojejunostomy, was done in 115 cases with a mortality of 5.2 per cent.

The mortality in cholecystectomy at present is higher for several reasons: It is done chiefly in those cases which have marked pathological lesions that have rendered useless the gall-bladder; or in septic cases with an empyema or gangrenous gall-bladder; so aside from the severity of an operation which extirpates rather than opens, the operative risk is greater, due to the pathological conditions which necessitate it. Cases requiring cholecystectomy, aside from acute conditions, are more often older and seriously damaged organically by long standing disease.

In 40 cases of cholecystostomy there was one death.

Most cases showed adhesions at operation. In the simple gall-bladder group 24 cases had adhesions between the gall-bladder, duodenum and stomach, and 14 cases between the gall-bladder and great omentum. In this series 44 per cent. had adhesions, of which over half were between the gall-bladder, stomach and duodenum. In the common duct group 65 per cent. had adhesions, 46 per cent. of which were between the gall-bladder and omentum, and in the pancreatic group 34 per cent. had adhesions, three-fourths of which were about the gall-bladder, including stomach, duodenum, or hepatic flexure with the gall-bladder and liver.

Stones were found at operation in 70 per cent. of all cases. As mentioned above, we may have severe gall-bladder disease with jaundice and toxæmia without stones.

In those cases showing marked infection of the common duct with pus formation, symptoms of cholangeitis were present—the infective organisms spreading up the hepatic ducts into the finer radicles of the liver, producing there enlargement and marked toxic symptoms. These cases are bad surgical risks. Death in these cases is due to cessation of liver function, and exhaustion and hemorrhage from blood changes. Operation is fraught with a high immediate mortality and delay is equally dangerous, as pus under pressure must be evacuated. The only safe procedure is a preventive one of removing the disease while it is yet in the gall-bladder.

The cultures taken from the bile and pus showed *Bacilli coli communis* most frequently.

The most common accompanying lesion was in the appendix, which was removed in 80 cases. Most of these showed chronic interstitial and obliterative appendicitis. There is a marked relation between chronic appendicitis and gall-stone disease, and in this series 80 cases gave symptoms of a long-continued discomfort in the appendiceal region.

The pathological findings of gall-bladders removed showed a preponderance of chronic interstitial cholecystitis in all groups with acute exacerbations of the same lesion next in frequency.

In this series I encountered six cases who had had previous operations for gall-bladder disease, for failure of which the present operations were performed. In four of these cases a cholecystostomy was done at the primary operation, and in two cholecystectomy had been done. The recurrence of symptoms in the cholecystectomy cases were due to pancreatic disease and improved on drainage of the common duct. Reoperations in the cholecystostomy cases were due to persistent fistula, or recurrence of symptoms, the latter being caused by reinfection, the reformation of stones or possibly by stones undiscovered at the primary operation.

In two cases cholecystectomy and choledochostomy were made, and in two cholecystoduodenostomy was indicated by pancreatic obstruction. All have recovered with marked immediate improvement.

CONCLUSIONS

1. Gall-bladder disease is preëminently a disease of the middle-aged female, but is by no means confined to that age or sex.

2. The early diagnosis can be made only by familiarity with a different symptomatology than that found in our text-books. The lighter grades of dyspepsia with localizing signs, however slight, in the epigastrium or right hypochondrium must be regarded as very suspicious of the beginnings of the gall-stone disease.

3. Gall-stones are merely the terminal stage and by no means the uniform accompaniment or most dangerous factor involved in gall-stone disease.

4. Infection as the cause, not only of gall-stones, but of the local and systemic damage of the disease, is the essential thing to recognize and treat.

5. The X-ray in diagnosis is dangerous therefore, not only because it fails to show a large percentage of stones, but because it emphasizes the importance of the calculous element of the disease, and if allowed to serve as an indication for operation will deprive many of the early treatment which alone is safe and efficacious.

6. Cholecystectomy is the operation of choice in obviously diseased gall-bladders, with drainage of the common duct in practically all cases, but particularly in those giving evidence of cholangeitis or pancreatic involvement.

GALL-BLADDER STATISTICS

Simple gall-bladder disease ..... 87 cases
Gall-bladder and common duct ..... 20 cases
Gall-bladder and pancreas ..... 52 cases

Age at Operation

	Average	Oldest	Youngest
Gall-bladder disease	45	70	20
Gall-bladder and common duct	47	75	19
Gall-bladder and pancreas	42	63	21

SIMPLE GALL-BLADDER DISEASE

	Case	Per cent.
Under 20 years	1	1.14
20 to 30 years	9	10.3
31 to 40 years	21	24.1
41 to 50 years	32	36.8
51 to 60 years	15	17.2
61 to 70 years	7	8.
71 and over	2	2.2

GALL-BLADDER AND COMMON DUCT

	Case	Per cent.
Under 20 years	1	5
21 to 30 years	1	5
31 to 40 years	3	15
41 to 50 years	8	40
51 to 60 years	3	15
61 to 70 years	3	15
70 and over	1	5

GALL-BLADDER AND PANCREAS

	Case	Per cent.
Under 20 years	0	00.
21 to 30 years	4	7.5
31 to 40 years	17	33.
41 to 50 years	24	46.1
51 to 60 years	6	11.5
61 to 70 years	1	1.9
70 and over	0	00.

SIMPLE GALL-BLADDER DISEASE

Males, 13 (average age 47) ..... 14.9 per cent.
Females, 74 (average age 44.3) ..... 85.1 per cent.

GALL-BLADDER AND COMMON DUCT

Males, 8 (average age 44.8) ..... 40 per cent.
Females, 12 (average age 49.2) ..... 60 per cent.

GALL-BLADDER AND PANCREAS

Males, 16 (average age 39) ..... 30 per cent.
Females, 36 (average age 39) ..... 70 per cent.

CASES OF GALL-STONE DISEASE

Females Beyond Forty-five, or Accepted Age of Menopause

SIMPLE GALL-BLADDER DISEASE

Above 45 years of age .....34 45.9 per cent.
Under 45 years of age .....40 54.1 per cent.

GALL-BLADDER AND COMMON DUCT

Above 45 years of age .....11 55 per cent.
Under 45 years of age ..... 9 45 per cent.

GALL-BLADDER, PANCREATIC INVOLVEMENT

Above 45 years of age .....15 41.6 per cent.
Under 45 years of age .....21 58.4 per cent.

Operated Cases

SIMPLE GALL-BLADDER DISEASE

Recovered ..... 83 95.5 per cent.
Died ..... 4 4.5 per cent.
1. Post-operative pneumonia, peritonitis ..... 2 weeks after operation
2. Carcinoma gall-bladder ..... 2 days after operation
3. Cardiac dilatation ..... 1 day after operation
4. Peritonitis..... 5 days after operation

GALL-BLADDER AND COMMON DUCT

Recovered ..... 19 95 per cent.
Died ..... 1 5 per cent.
Hemorrhage .....13 days after operation

GALL-BLADDER AND PANCREAS

Recovered ..... 45 85.5 per cent
Improved ..... 2 5.0 per cent.
Died ..... 5 9.5 per cent.
1. Partial obstruction ..... 2 months after operation
2. Hemorrhage ..... 9 days after operation
3. Heart failure ..... 9 days after operation
4. Failure respiratory centre, stovaine ..... on table
5. Carcinoma, pancreas ..... few hours

CHOLECYSTECTOMY

Simple gall-blader disease:
Cholecystectomy alone or combined with other operations .....64 cases
With 3 deaths, 4 per cent.
Gall-bladder and common duct:
Cholecystectomy alone or combined with other operations .....18 cases
No deaths.
Gall-bladder and pancreas:
Cholecystectomy alone or combined with other operations .....14 cases
With 2 deaths, 3 per cent.
Gall-bladder, common duct and pancreas:
Cholecystectomy with other operations .....19 cases
With 1 death, 1.3 per cent.

SIMPLE GALL-BLADDER DISEASE

	Cases	Deaths
Cholecystectomy	19	2
Cholecystectomy, appendectomy	43	1
Cholecystectomy, gastrojejunostomy	1	
Cholecystectomy, ileocolostomy	1	
Cholecystostomy	14	1
Cholecystostomy, appendectomy	14	

GALL-BLADDER AND COMMON DUCT

	Cases	Deaths
Cholecystectomy, choledochostomy	18	
Choledochostomy alone	1	1
Cholecystoduodenostomy	1	

GALL-BLADDER AND PANCREAS

	Cases
Cholecystectomy and appendectomy	8
Cholecystectomy	6
Cholecystostomy and appendectomy	6
Cholecystostomy	5

OTHER OPERATIONS AT SAME TIME

Simple gall-bladder		Gall-bladder and common duct		Gall-bladder and pancreas	
Appendectomy	45	Appendectomy	10	Appendectomy	25
Oophorectomy	3	Umbilical hernia	1	Tubes and ovary	2
Myomectomy	2			Right Inguinal hernia	1
Ileocolostomy	1			Pancreas drained	1
Salpingectomy	2			Incisional hernia	1
Hernia	1				

ADHESIONS AT OPERATION

SIMPLE GALL-BLADDER DISEASE

	Cases
Omentum and liver	21
Duodenum and stomach	27
Hepatic flexure	4

Forty-four per cent. showed adhesions with 61 per cent. to stomach and duodenum.

GALL-BLADDER AND COMMON DUCT

	Cases
Gall-bladder, stomach, duodenum, liver	4
Omentum and gall-bladder	6
Liver and duodenum	1
Gastrohepatic omentum and liver	2

Sixty-five showed pericholecystic adhesions, 46 per cent. between gall-bladder and great omentum.

CASES OF GALL-STONE DISEASE

GALL-BLADDER AND PANCREAS

	Cases
Stomach and duodenum	12
Omentum	11
Liver and duodenum	8
Hepatic flexure	1
Around pancreas	3

Thirty-four per cent. showed adhesions of stomach and duodenum.

Laboratory Reports

	Simple gall-bladder	Gall-bladder and common duct	Gall-bladder and pancreas
Hæmoglobin average	82.8	79	81.6
Red blood-cells average	4,593,820	4,850,000	2,665,416
White blood-cells average	9,035	9,145	9,480
Polymorphonuclears	68.9	75.2	70
Coagulation time	13 min.	7.5 min.	9.8 min.
Low	1.5 min.	3 min.	1
High	4.6 min.	13 min.	14

Stomach Contents

	Simple gall-bladder			Gall-bladder and common duct			Gall-bladder and pancreas		
	Average	Low	High	Average	Low	High	Average	Low	High
Free HCl	16	0	67	16	0	80	16	0	51
Total HCl	41	0	102	39	4	150	41	16	103

Pathological Diagnosis

SIMPLE GALL-BLADDER

Chronic interstitial cholecystitis	46 cases	65 per cent.
Chronic suppurative	4 cases	
Gangrenous	7 cases	
Acute interstitial	2 cases	
Chronic catarrhal	3 cases	
Adenocarcinoma gall-bladder	2 cases	

GALL-BLADDER AND COMMON DUCT

Chronic interstitial cholecystitis	13 cases
Chronic catarrhal	1 case
Acute interstitial	2 cases
Gangrenous	1 case

GALL-BLADDER AND PANCREAS

Chronic interstitial cholecystitis	20 cases
Chronic Catarrhal	4 cases
Suppurative	1 case

FISTULOUS COMMUNICATION BETWEEN THE STOMACH AND COLON, FOLLOWING GASTRO-ENTEROSTOMY *

By Carl A. Hamann, M.D.
of Cleveland, O.

Dr. C. aged sixty years had for many years a duodenal ulcer, as shown by all the characteristic symptoms and signs. At the operation on December 19, 1910, a large callous ulcer involving the first part of the duodenum was found. A posterior, "no-loop" gastro-enterostomy was done, followed by recovery of health for a period of several months. Then he began to have hæmatemesis and bloody stools again.

On May 15, 1911, five months after the first operation, the ulcerated part of the duodenum with a small part of the stomach was excised.

He then enjoyed pretty good health for about two and one-half years when, after a severe straining effort in running his automobile, he had severe pain followed by intestinal hemorrhage. After this he continued to suffer, the main symptoms being loss in weight and strength, diarrhœa, loss of appetite and a fecal odor from gastric eructations; there was also considerable visible peristalsis.

An X-ray examination after the ingestion of a bismuth meal showed a rather confused picture which we could not clearly interpret.

On account of the patient's condition, extended X-ray observations were not considered advisable, but the following facts were obtained.

"The bismuth-meal passed rapidly from the stomach through the gastro-enterostomy opening into an enormously distended jejunum, and into the blind end of the duodenum which was likewise distended to almost three inches in diameter. From this location the path of the bismuth-meal could not be accurately determined on account of the marked distention of portions of the small bowel. However, part of the bismuth could be seen disseminated in these coils. A careful study of the radiographs made in the light of the operative findings showed that a small amount of bismuth had entered directly from the jejunum into the colon. The distended condition of the small bowel indicated that there

* Read before the American Surgical Association, June 10, 1915.

had been a marked degree of intestinal obstruction." (Dr. Geo. F. Thomas.)

On December 31, 1914, he was operated upon for the third time. There was found considerable thickening about the gastro-enterostomy opening, and the transverse colon was adherent to the stomach and jejunum. A finger could be passed from the stomach into the small intestine and also into the colon; there was some dilatation of the jejunum on the distal side of the anastomosis, and also of the colon on the proximal side of the gastrocolic fistula. There was no ulcer.

The adherent viscera were separated from one another, the gastric and jejunal openings were closed and about four inches of the transverse colon were resected, as the gut was much contracted at the point of adhesion to the stomach; the operation was completed by making an anterior gastrojejunostomy.

On the fifth day after the operation he passed considerable blood per anum, and later on it became necessary to resuture the abdominal wall. Complete recovery occurred and, at present, six months after his last operation, he is enjoying good health.

To summarize the main facts in connection with the above case: Posterior gastro-enterostomy, for duodenal ulcer, followed in five months by partial resection of stomach and duodenum, ncessitated by recurring hemorrhage; a period of good health for two and one-half years; then, after a severe strain, another hemorrhage, which was followed by a period of several months of ill-health, characterized by loss in weight and strength, diarrhœa, and by eructations from the stomach which had a fecal odor. A third operation at which there was found a gastrocolic fistula. Separation of stomach, jejunum and colon from one another, closure of the openings in stomach and jejunum, resection of part of transverse colon and the making of a new (anterior) gastro-enterostomy. Recovery with restoration of health.

The formation of the gastrocolic fistula was due, no doubt, to a gastrojejunal ulcer, following gastro-enterostomy, around which adhesions formed between the stomach and colon and later a fistulous communication between the stomach and colon was gradually established.

According to Voorhoeve [1] the first case of gastrocolic fistula was described by Haller in 1755; Hilgenreiner [2] stated in 1912 that the number of recorded cases was 119.

The cause of these fistulæ is nearly always some gastric affection, such as carcinoma or ulcer, which, secondarily, after adhesions to the colon have formed, results in perforation of the walls of the large intestine. Since the introduction of the operation of gastro-enterostomy,

there has been added another factor, namely gastrojejunal, or peptic ulcer of the jejunum, which may, by perforating into the colon, produce the lesion under discussion. There is thus found, in some cases at least, what may be described as an indirect fistula between the stomach and colon, the peptic ulcer of the jejunum perforating into the colon in close proximity to the gastro-enterostomy opening. However, the disturbance produced and the symptoms of such a gastrojejunocolic fistula are practically the same as those of a gastrocolic fistula.

Patterson in 1909 collected 114 cases of peptic ulcers of the jejunum, following gastro-enterostomy; 5 of these perforated into the colon. Hilgenreiner (*loc. cit.*) in 1912 added 8 more from the literature.

The chief symptoms of gastrocolic fistula are three in number, viz.: fecal vomiting or eructations of foul-smelling (fecal odor) gases, without other signs of intestinal obstruction, diarrhœa, or lienteric discharges, and loss in weight. That these symptoms should occur is obvious and their explanation is equally plain. Other evidences of the condition are the ability to inflate the stomach from the rectum, the vomiting of enemas, the withdrawal by gastric lavage of colored fluid introduced into the rectum, and the finding of pepsin and hydrochloric acid in the fæces. None of these symptoms are, however, constantly found.

The size and position of the opening, its possible valve-like character, the condition of the pylorus and other factors may cause variations in the symptoms in different cases. It has been pointed out, for instance, that in case of pyloric stenosis, if a gastrocolic fistula forms, the former vomiting may cease, as the gastric contents then pass into the colon; also if the position and size of the fistula are such that the food cannot readily enter the colon, the stomach will remain filled for a time and fæces cannot enter it; in case of a large opening, fecal vomiting may be absent because the food more readily enters the colon, and, *vice versa,* the fistula may be too small to allow fæces to enter the stomach.

In recent years, X-ray examination has afforded aid in the diagnosis. Voorhoeve (*loc. cit.*), Neumann,[3] Haudek[4] and others have described the radiographic findings.

After a bismuth meal the ingested material may be seen to enter the colon directly, the stomach not filling up as normally is the case; the rapid filling of the descending colon and sigmoid is also to be observed. It may be possible to force the material from the stomach into the colon, and *vice versa,* by external pressure; the simultaneous presence of bismuth in the small intestine and the distal parts of the colon, the proximal

portions of the colon being free or nearly so from bismuth, may be observed.

Upon injecting bismuth into the rectum, it passes into the stomach or by external pressure it may be forced there. Bismuth may be found in the small intestine, after a rectal injection, showing that it has entered from the stomach, for normally, when a rectal injection is made it does not pass beyond the ileocæcal valve. The increase in size of the *Magenblase* may also be observed when air is forced into the rectum (Voorhoeve).

When there is a gastrojejunocolic fistula, as is perhaps usually the case when gastro-enterostomy has been done and a gastrojejunal ulcer is the cause of fistulous communication with the colon, the X-ray picture is rather confusing and hard to interpret, as in my case.

The treatment of gastrocolic and gastrojejunocolic fistulæ naturally consists in separating the adherent viscera from one another, and closing the openings in each; resections and entero-anastomosis or other procedures may become necessary, depending upon the peculiarities of the individual case.

Hilgenreiner (*loc. cit.*) has collected 11 cases in which operation was done, two of which were fatal.

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PAGET'S DISEASE OF THE NIPPLE AND ALLIED CONDITIONS*

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Paget's disease of the nipple, as it is commonly designated, derives its name from the brief contribution in *Saint Bartholomew's Hospital Reports,* vol. x, 1874, by Sir James Paget, under the title of "Disease of the Mammary Areola Preceding Cancer of the Mammary Gland." Since that time it has received a number of other names, usually framed by their originators to indicate its true pathological nature, or what they supposed this to be, but so far without displacing this as the common title under which it is indexed and described. To Paget belongs the credit for bringing it to the attention of the profession in the clear, concise description of the appearance and clinical course of the malady, a description which, in its essential features, is difficult to improve upon, although later studies have enabled us to contribute much to our knowledge of the variations and modifications which location and time of observation may make in its clinical course and macroscopic appearance, while an apparently unending stream of contributions on the histo-pathology of the disease has flowed through the literature from that time down to the present day. Indeed, it would seem to have engrossed, in view of its rarity, an amount of time in the minds of dermatologists, pathologists and surgeons out of all proportion to its importance, the reasons for which we will return to later.

While credit is usually given to Paget for the first description and while the judgment of time has continued to designate it by his name, yet, as Wiggin and Fordyce point out, the disease had been described many years before by Velpeau. We have copied from the *Leçons Orales de Clinique Chirurgicale,* in the section on Diseases of the Female Breast, the following paragraph:

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Degenerescences Croûteuses—Le mamelon se couvre quelquefois d'une affection squammeuse, tenant le milieu entre l'eczéma chronique et la psoriasis. Je l'ai observée deux fois chez dames qui avaient depuis long temps cessé d'allaiter. Les croûtes qui recouvraient l'organe étaient d'un gris verdâtre dans un cas, d'un gris jaunâtre dans l'antre, assez épaisses, fendillées et adherentes. D'es qu'on cherchait à les détacher, on voyait survernir sur les petites plaies un suintement sanguin assez abondant.

He adds that the affection is often accompanied by an itching that is almost insupportable, that compels the bearer to scratch and affects the general health. It lacks the ordinary signs of inflammation. Velpeau traces its source to irritation of the nipple by rubbing against the underwear or the corset, and says that while it is frequently cured by the use of a white precipitate ointment, as in one of his cases, it may sometimes, when of long standing, resist any treatment short of amputation of the nipple, which was the outcome in the other case. We have quoted Velpeau's description and views of what were apparently cases of the lesion under discussion because we have encountered the barest mention of his name in connection with the subject.

Paget's article was based upon 15 cases personally observed by him and, since that time, there have been reported in the neighborhood of 140 cases, not a large number for 40 years when one considers the frequency of breast lesions and of dermatological affections in general. By no means all of these cases were operated upon and many of the important contributions to the pathology of the subject and many of the theories as to its origin and true nature, including its relationship to breast cancer, have been founded upon the study of two or three cases, and these studies sometimes with and sometimes without a careful analysis of previous contributions, and a consideration and weighing of the work done by eminent and skilled investigators on the same subject. In the meantime, and since it was first described by Paget, the pendulum of opinion as to the primary or secondary nature of the disease has swung back and forth, and theories have been formulated, and forgotten, and revived without arriving at any unanimity of opinion, until the present time, when the unprejudiced observer will find that dermatologists and surgeons, including in the latter group surgical pathologists, are arrayed on opposite sides of the main question, and that there exist in each group minor differences of opinion besides. We have been fortunate enough to secure a number of specimens from cases of Paget's disease and conditions closely simulating it, including five cases which we would positively identify as true Paget's, and in view of the lack of unanimity

of opinion among pathologists, and the vagueness of the views held by many clinicians, as well as the fact that, as pointed out, this is a relatively large amount of material, we have been led to report the results of our studies in some detail, and to abstract and analyze the work done by previous investigators. We are indebted to Doctors Edward Martin, Charles H. Frazier, William L. Rodman, George M. Laws and W. C. Clarke for the loan of material and permission to publish their cases. The specimens from these cases and from our own have been studied in Dr. Speese's Laboratory of Surgical Pathology in the University of Pennsylvania.

It may not be amiss to dwell here on the reasons which have led to so great an amount of interest in what is in reality a rare disease, for that true Paget's disease is rare, all authorities agree, and fortunately some figures are available to prove this assertion. G. T. Jackson stated that in the statistics of the American Dermatological Association from 1877 to 1893, which embraced 204,866 cases, there were none of Paget's disease included, while in 1894 there was one case in 24,321. He collected 45 cases reported up to 1896 but did not claim that this embraced all cases in the literature. Hannemuller and Landois in 1908 stated that about 100 cases had been published up to that time and Reuter in 1912 found about 130 cases, while Dr. Joseph MacFarland of Philadelphia, who has also been pursuing some studies on the subject, informs us that he has references to about 150 cases to date. It will be seen that the number of cases grows steadily but slowly. M. B. Hartzell in 1910 collected 18 cases of extramammary Paget's disease, and we have not found any later estimate of the number of cases to be added to this class.

The reason for the great amount of interest taken in the disease undoubtedly lies in the hope that has been stimulated from time to time that in its study may be found a sequel to the cancer problem. Paget's paper, pointing out as it did that cancer followed closely on the heels of what he believed to be ordinary eczema or psoriasis occurring on the nipple and areola, and the comparisons which he drew to the development of cancer on other parts of the body which are the sites of chronic irritations, and the deductions which he made as to the dependence of such malignant changes for their origin on the chronic irritations described, was calculated to instil this hope. The first histological studies were those made by Butlin and George Thin. Butlin studied four cases operated by Paget, Savory and Smith, and thought he could trace a direct relationship between what he still interpreted as eczema on the surface, and carcinomatous changes de-

veloping secondarily, while Thin was the first to demonstrate the sharp distinction between the skin changes and true eczema, and also the first to claim, as a result of his studies of six cases, that the superficial lesion was secondary to duct carcinoma, which caused connective tissue destruction in the skin by the action of what he called a connective tissue poison, viz., cancerous epithelium. This explanation of Paget's disease was not accepted by Duhring and Wile, whose studies were prosecuted soon after, and who made another notable contribution based thereon. The next stage in the history was that marked by the startling claims of Darier and Wickham, who were impressed by the peculiar nature and appearance of the cells in the deeper layers of the epiderm, which are now recognized as characteristic of this affection, and believed that they were able to identify in them the psorosperms or coccidia which were the cause of the accompanying malignant disease of the breast. The inference was naturally drawn from such a claim of discovery that the long sought for cause of cancer was here uncovered. Further histological studies soon showed, however, the true nature of these cell forms to be the actively dividing, deeply-staining nuclei, and the changes produced by fixing agents in the œdematous cells of the rete mucosum, and the compression and alterations in shape and location of other cells in their immediate neighborhood, with the bizarre picture so produced.

The overthrow of Darier and Wickham's theories was marked by a return to the views of Duhring and Wile, and first Karg and then Unna recognized in Paget's disease, as Thin had said years before, an affection differing from any other known skin disease, entirely unlike eczema or psoriasis or any ordinary catarrhal process, Karg regarding it as a superficial malignant process marked by œdema of the prickle cells, while Unna looked on it as a unique affection differing as widely from cancer as from eczema. Thin had almost from the beginning regarded the characteristic epidermal changes as secondary to duct cancer, as he called the impactions in and infiltrations extending from the lactiferous ducts, while Ely had made similar deductions in the study of the first case reported by G. T. Jackson, deductions which were vigorously combated in the discussion before the American Dermatological Association. It was mainly due, however, to the paper of Jacobaeus, followed up and supported by the articles of Schambacher, Ribbert and Kyrle, that the present day conception of Paget's disease as a secondary manifestation of breast cancer is due, a conception which is not shared by dermatologists, and whose upholders are by no means in unison when they come to the question as

to how the various changes in the epiderm and corium are produced. To the dermatologist to-day, Paget's disease appears as it did to Duhring, Karg and Unna. Sequeira, Stelwagon, Hartzell, Knowles and other authorities regard it as a peculiar affection, primary in nature, not confined to the breast but occurring in any locality, of rare occurrence, by some classified as frankly malignant and by others as showing no true characteristics of malignancy in its histology but followed sooner or later in a large percentage of cases by the development of malignant disease in the underlying tissues.

We have outlined the history of this interesting lesion in an attempt to show the interest which has always attached to a subject which occupies a borderline position between surgery and dermatology. We would add here that our own studies have led us to adopt the views of the dermatologists and to regard it as a primary condition, whether occurring in the breast or other regions, views which have been adopted by those men who have been thoroughly trained by the study of the histology of skin affections, and who have not only paid close attention and given due weight to the clinical as opposed to the purely pathological aspects of the question, but who have had the opportunity, not frequently offered to surgeons, to study the lesion in other parts of the body where its histology is not obscured by changes in the mammary gland, which are notoriously baffling and confusing and require long experience to properly interpret.

The clinical picture of Paget's disease when it involves the nipple is well known, and it would seem that it should not admit of misinterpretation when fully developed. It has been remarked by others that the description of Paget holds as true to-day as when it was penned by that master of surgery, and this is true although the study of many cases since has naturally enabled us to add to it and fill in many details and to describe better its beginnings and its variations from the classical type. He says, " The patients were all women, varying in age from 40 to 60 or more years, having in common nothing remarkable but their disease. In all of them the disease began as an eruption on the nipple and areola. In the majority it had the appearance of a florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed; like the surface of very acute diffuse eczema, or like that of an acute balanitis. From such a surface, on the whole or greater part of the nipple and areola, there was always copious, clear, yellowish, viscid exudation. The sensations were commonly tingling, itching and burning, but the malady was never attended by disturbance of the general health." It

is not improbable that Paget made the mistake, not uncommon to-day, of including in his series some cases which were not true examples of this affection, but were cases of scirrhous carcinoma with secondary skin involvement. For example, when he goes on to speak of less frequent types which he has seen: "In some of the cases the eruption has presented the characters of an ordinary chronic eczema with minute vesications, succeeded by soft, moist yellowish scabs or scales and constant viscid exudation. In some it has been like psoriasis, dry, with a few white scales slowly desquamating, and in both these forms, especially in the psoriasis, I have seen the eruption spreading far beyond the areola in widening circles or with scattered blotches of redness, covering nearly the whole breast." The latter part of this quotation might be used to describe certain rare types of diffuse carcinoma of the breast, which do not at all resemble in their pathological and microscopical features true cases of Paget's. We have recently encountered a very early case of diffuse carcinoma of this type, in which there were associated with a dry and limited eczema of the nipple and long standing retraction of the same, widening circles or portions of circles of reddening in the skin, at a little distance from the nipple, resembling telangiectatic areas, without ulceration of the nipple and without tumor formation clinically, the breast being only slightly larger and heavier than the opposite side, but in which, after amputation had been performed, the microscope revealed very early and diffuse scirrhous carcinoma. In this case we made the mistake of suspecting Paget's disease (Fig. 2).

M. A., sixty-eight years, a widow; two children, one living. A sister died of cancer of the breast. The left breast had adways been small and rather hard and the nipple somewhat retracted. Four months ago noted some reddening of the overlying skin and increased hardness of the gland. No pain. Examination shows a diffuse pinkish redness of the skin over the breast, patchy in distribution, and some roughening of the areola. The breast seems slightly larger and heavier than the opposite side and denser, but not with the stony irregular hardening of cancer but of an elastic or springy density, and it is only slightly more tender than the right breast. There is no discharge from the nipple and no fixation of the breast on the underlying muscles. No lymph glands are palpable in the axilla. The patient has lost twenty pounds in the last year, and has 1½ per cent. of sugar in the urine. Operation was advised, and performed a few days later under gas-oxygen anæsthesia. The breast was removed with the overlying skin and the pectoral fascia. Macroscopic examination by

Dr. Speese in the operating room showed no evidences of cancer. The axilla was therefore not dissected nor the muscles removed. In this case, an erroneous diagnosis of Paget's disease was made before operation.

Pathologic Examination.—5678. Specimen consists of a breast with slightly inverted nipple and showing several concentric rings, red in appearance about the areola. There is no distinct excoriation present, although the skin appears scaly. On cross-section through the breast the tissues are dense and fibrous in nature and the entire breast is the seat of this transformation. The tissue cuts with a slightly increased sense of resistance, the entire picture resembling the fibrous type of chronic cystic mastitis. While the gross appearance did not suggest malignancy at the time of operation the breast was amputated on account of the patient's age and the diffuse fibrous overgrowth.

Microscopic Examination.—The fibrous tissue when examined was infiltrated by a scirrhous carcinoma in a small area situated beneath the nipple and 4 cm. from the surface. Elsewhere the usual picture of a chronic cystic mastitis was present. In the subcutaneous tissues in areas covered by the reddened skin, an interesting picture is noted; here small plugs of epithelial cells are found in the lymphatics, the process resembling a lymphatic metastasis extending from the malignant area below and travelling toward the skin. These emboli are numerous and three and four may be found in a single field (Fig. 4), but in no instance are they noted invading the skin.

The process represents a form of carcinoma diffuse in nature, rarely encountered and difficult to recognize grossly because it was found in a breast the seat of chronic cystic mastitis. The malignancy was so early that the distinct gross manifestations of cancer had not appeared. The metastatic emboli may be the beginning of a cancer *en cuirasse,* and it is noteworthy that they were found only in the subcutaneous tissues covered by the reddened skin.

In the very early stages of the disease, the lesion shows itself as a small, indurated area, covered perhaps by a crust or scurfy covering, the nipple slightly reddened around it, and a little itching or burning as subjective symptoms. As it spreads, the ulceration, which is accompanied by connective tissue inflammation and which separates it sharply from eczema and psoriasis, becomes more apparent, and, while scabbing may be present, beneath the incrusted detritus and dried secretions the characteristic appearance, as described by Paget, will be found. A very characteristic appearance is furnished by those cases in which bluish-white areas of epiderm deck the surface here and there, while the boundary edges of the ulcer are sharply defined. Beneath the surface of the ulcerated area is a characteristic thin, flat area of infiltration, somewhat chancre-like in its density, and when pinched between thumb and finger has been likened by English writers

in its feel to a penny felt through a cloth. The nipple itself becomes flattened and undergoes, in time, absorption by ulceration or, when cancer develops early in the breast, it soon undergoes characteristic retraction due to traction on the milk ducts. These changes may extend over months and years. In very long standing cases the disease spreads slowly from the areola over the skin of the breast, even perhaps to the axilla, and may exist for five, ten, fifteen or even twenty years without seriously affecting the general health or presenting those evidences of deeper malignant disease of the breast which Paget saw in all his cases which he followed, and which usually develop in two or three years and which are the common but perhaps not inevitable ending.

It is commoner in married than in single women and affects the right breast oftener than the left, is very rare in the male breast, but has been described there. In the later stages a tumor develops in the underlying gland, usually beneath the nipple, which tumor varies in size with the stage of the disease, and is followed by axillary enlargements and the usual evidences of cancer.

The above description holds true of the great majority of cases of Paget's disease, but there are exceptions. The most significant of these is that a goodly number of typical cases, fulfilling all the demands which a microscopic diagnosis entails, are found in other parts of the body. Duhring, Fordyce, Dubreuilh, Fox and MacLeod, and others have written critically and more or less extensively on this phase of the subject and M. B. Hartzell collected, in 1910, 18 cases of extramammary Paget's disease. Among the regions affected were the scrotum and penis, glans penis, perineum, vulva, pubic region, umbilicus, axilla, neck, nose, lower lip, buttock and arm. Nine of these cases were on the external genitalia or adjacent parts, including five on the glans penis. When it arises in the axilla it may spread to the breast, the reverse of the usual course, and as in Jungmann and Politzer's case may, after a course of nine years, terminate in a pavement-cell carcinoma in that site. It is now marked by a rapid and now by a chronic course. It may affect the virgin or the multiparous woman. A family history of cancer is not common. Both breasts have been seen to be involved and it has developed in the remaining breast after one has been removed for tumor. Whatever the clinical course and symptoms may be, or may simulate, the histological examination either confirms or refutes the diagnosis.

Cases of simple eczema of the nipple, of primary carcinoma of the breast with excoriation or ulceration and destruction of the nipple or of the skin in its neighborhood, papillary cystadenoma attended by

discharge from the nipple, the rare form of diffuse carcinoma with early involvement of the skin of the type which we have mentioned, and one or more types of the very rare primary tumors of the nipple as reported and collected by Battle and Mayberry, Linfors and Schreiner, may cause errors in diagnosis. The commonest error would seem to be the inclusion of cases of ulcerating scirrhus, and this conclusion we have reached as a result of our study of a number of these cases, in several of which a diagnosis of Paget's disease had been made by a very distinguished surgeon, in some of which the clinical history was strongly suggestive and in some of which it was entirely lacking. It has only been after the study of many dozens of sections of tissues in some of these cases, that we have been forced to discard them as examples of Paget's disease or malignant papillary dermatitis, as it is sometimes called.

We have already quoted Paget's original description of the clinical appearance and symptoms. He distinctly states that he saw no difference in the process from long standing eczema or psoriasis. As to the cancers which follow, he states that he saw in them nothing peculiar or differing from ordinary cancer in the course they pursued. The noteworthy fact has been their development following a chronic irritation which he likens to the persistent "rawness" which may precede cancer on the glans penis, and the chronic irritation on the lower lip and the superficial syphilitic disease of the tongue, which are followed by cancer in these localities. The superficial disease induces a degeneration in the very susceptible sites mentioned, which causes them to become the seat of cancer, and he mentions the pylorus, ileocæcal valve and rectum as perhaps being affected in a similar manner from similar surface irritations.

The first histological studies of Paget's disease were made by Butlin, who examined four cases. He noted the epithelial proliferation in the ducts as well as the changes occurring in the skin, and demonstrated the presence of carcinomatous infiltration in the breast itself. He believed that there was a definite relationship between the "eczema" and the cancer, and that the former produced a proliferation in the mucous layer of the epiderm. The process then extended from the skin to the milk ducts and thence to the smaller ducts and acini, and finally terminated as cancer.

George Thin first called the disease malignant papillary dermatitis. He studied 6 cases and described the usual cell changes due to degeneration, including vacuolation, etc. He distinguished the affection from eczema by the history, the well-defined margin and the infiltration

of the papillary layer. He pronounced it different from any known skin disease, and, as already mentioned in speaking of the history of this subject, concluded, as the result of his studies, that the process was secondary to duct carcinoma and was caused by some irritating agency arising in the ducts. He distinguished the cancer which developed from ordinary scirrhus.

Duhring and Wile emphasized the encroachment on and obliteration of the papillæ of the corium by the downward proliferation of the cells of the rete. They believed that the disease was an abnormal epithelial cell proliferation beginning in the rete Malpighii, which extends secondarily to the milk ducts and spreads downward to the deeper ducts, breaks through their thinner walls, and as cancer spreads upward toward the skin surface.

Darier and Wickham added to our knowledge of the clinical features as to time of development, early symptoms and anatomical features. They emphasized important points in differential diagnosis and described the histological appearance of Paget's disease on the breast as well as elsewhere. They believed the affection was due to psorosperms or coccidia which they described in the deep layer of the epiderm.

Bowlby, as a result of his study of a large number of cases, demonstrated the fact that there was a definite histologic picture of Paget's disease as described by his predecessors, and looked upon the affection as precancerous and not in itself malignant.

Karg regarded the condition as a superficial cancer and described the active proliferation of epithelium in the skin in advanced cases, with a breaking through into the underlying tissues.

Unna, in presenting one of the most satisfactory descriptions of the pathology of Paget's disease, definitely disproved the psorosperm theory of Darier and Wickham. He regards it as a unique lesion, not primarily malignant, but comparable with such other dermatoses, precancerous in nature, as xeroderma pigmentosa and sailor's skin. It is as different from cancer as it is from eczema and, while it does not lead directly and necessarily to cancer, it prepares the ground for it so thoroughly that cancer develops in most cases. Like Duhring, Wile and Karg, he recognizes the typical and important changes in the shape of peculiar degenerations of the prickle-cells which he regards as a peculiar form of epithelial œdema. The nuclear changes, loss of fibrillation, vacuolation due to the action of fixing agents, compression forms and diminished cornification, are all clearly described. The subepithelial infiltration, described by all investigators, he calls a bul-

wark and regards it as a defensive process. The cancer which follows may begin in the skin, the lactiferous ducts, or in the breast itself. He does not admit a direct transition of the skin disease into cancer.

Shields's case proved that a long standing lesion, involving an area covering the skin of the entire mammary region, could after seven years terminate in a squamous cell carcinoma without involvement of the glandular structure of the breast.

Fordyce has described clinical and pathological characteristics and, while looking upon the disease as a primary one when it occurs in the breast, favors the view that it is malignant from the start, and difficult to separate from certain types of epithelioma.

Dubreuilh, in reporting a case of Paget's disease of the vulva, looked upon the affection as a superficial epithelioma, which invaded the mucous glands in the same way it did the skin follicles, thus finding an early pathway to the deeper tissues which makes the disease more serious on mucous surfaces. He mentions the minor differences in its behavior on mucous surfaces as compared with the growth on skin surfaces.

George T. Jackson reported two cases which had been studied carefully, one by Ely and the other by Schultze. Ely regarded the process in the first case as secondary to a non-malignant type of breast tumor, probably a pericanalicular fibroma. Schultze looked on the process as distinctly inflammatory and not epitheliomatous. He said that in the present stage of our knowledge, the genetic connection between Paget's disease and carcinoma of the breast remained a matter of speculation, the processes being essentially different.

T. C. Fox and J. H. M. MacLeod reported a case of Paget's disease of the umbilicus of eleven years' duration and compiled an excellent résumé of the literature. They collected cases of extramammary lesions reported by Radcliffe Crocker, Darier and Couilland, M. Shields, Dubreuilh, Fordyce, Tarnowsky, Pick, Winfield and Ravogli. Fox and MacLeod agree that the histological changes described are characteristic and pathognomonic, regardless of where the lesion occurs. Also, that in their case there was no definite malignant change present, and they do not regard the process as primarily malignant but, like xeroderma pigmentosa, ordinary warts and pigmented moles, it is a precancerous lesion with malignant potentiality. They point out that it is both unproven and unlikely that the degenerated cells present in the epiderm can take on malignant characteristics, but think it more likely that a prolonged action of the same cause which produced the degeneration may in non-degenerated cells cause their reversion and proliferation.

They suggest that the process starts in the corium from some irritation beginning in the blood-vessels, either in response to locally implanted microörganisms or a poison produced by an irritant acting on the epidermal cells. The inclusion of a portion of Meckel's diverticulum in the umbilicus in their case was interesting but the congenital rest showed no malignant changes whatever.

The observations of Jungmann and Politzer indicate that the primary process is not necessarily a malignant degeneration of the cells in which Paget's disease begins, because the cancer which finally arises may occur not only in the epiderm but also in the glandular offshoots of the skin (follicles, etc.), in the ducts and in the glands of the breast. The case which they studied originated in the axilla as a small, red, moist spot, which gradually enlarged and in four years' time extended almost to the nipple and arm. Improvement followed X-ray treatment, after which sections were taken for microscopic examination, which showed that the process was a primary squamous carcinoma arising in the skin and extending to the axillary lymph-nodes. The authors were unable to state what the nature of the primary skin affection is but gave it the name of "dermatitis epithelialis circumscripta chronica eczemiformis."

The conclusions of Jacobaeus, based upon a study of three cases, have influenced many writers on the subject of Paget's disease. His explanation of the nature of the disease does not seem warranted in view of our present knowledge, both clinical and pathological. Jacobaeus concludes that Paget's disease is carcinomatous from the beginning, and arises in the gland epithelium of the ducts. The changes in the skin are due to proliferation, and extension into the skin, of cancer cells originating from glandular epithelium. The Paget cells are not locally degenerated epithelial cells, but metastatic cancer cells, and similar changes occur when the usual form of adenocarcinoma ulcerates through the skin. The late appearance of a cancer points to the benignancy of the primary affection, and is due in part to obstruction to the growth of the tumor exerted by the connective tissue and possibly the striated muscle. A direct connection between the Paget cells and the cancer cells was traced in two cases; this fact is substantiated by the fact that Paget's disease begins at a place where its primary origin can be traced back as well to gland epithelium as to the skin, for it arises where the ducts empty, and here the epithelium is modified.

Schambacher does not agree with the view that Paget cells represent locally degenerated cells of the skin; rather he regards them as not

arising in and having nothing in common with the epiderm. He states that the cells of the epiderm and Paget cells differ in many ways; they are separated sharply from one another, the Paget cells do not possess intercellular spines, and do not show the arrangement of squamous epithelium. He says the process is carcinoma from the beginning; it extends to the skin, causing compression and death of the epidermal cells, first attacking the lower layers. He explains the process by assuming that the cancer arises in the nipple, then extends to the skin and ducts, and finally blocks off the latter, causing the dilatation found in most cases.

Ribbert also regards the cancer in the ducts as the primary process. He did not find any tendency of the Paget cells in the skin to infiltrate the subcutaneous tissues and form a malignant degeneration. He noted in only a few places a connection between the Paget cells and the carcinoma.

v. Winiwarter believes it to be a special form of skin cancer with a characteristic course, and its relative benignity allies it to ulcus rodens, and states that these two rare forms mingle with each other and with other skin cancers and lead to numerous misunderstandings.

Kyrle also assumes that the breast tumor is the primary affection and the Paget cells in the skin represent the regionary metastases, the cells spreading in the lymph channels in a retrograde manner, *i.e.*, toward the nipple. This form of extension of a breast cancer is only a deviation of the type of extension seen in the lenticular form of cancer and in *cancer en cuirasse*. Kyrle concludes that Paget's disease has no common pathological and anatomical basis, for in one case a squamous cell carcinoma may be present, in another, a cylindrical cell or gland carcinoma, indicating that the disease may originate respectively in the nipple, the milk ducts or the parenchyma of the breast.

Hannemuller and Landois lay great emphasis upon the different morphology of the Paget and the cancer cells. They contrast the difference in size and staining properties, and state the two cells differ in type as much as is possible for any two varieties of cells. They think a retrograde metastasis must be assumed to account for the presence of these cells in the skin, but believe it is difficult to explain why only the squamous epithelium has received the invasion of cancer cells, while the underlying connective tissues remain free. They conclude, as the Paget cells only occur where the chronic granulation tissue comes in contact with the skin, that the latter is largely responsible for the changes induced in the cells, and that in consequence of the long continued secretion on the ulcerated surface, the cells become

so injured that a swelling of the protoplasm results through alterations in osmosis and diosmosis, finally causing the typical Paget cell.

Hirschel believes with others that cancer is primary.

M. B. Hartzell brought the number of cases reported in extramammary regions up to 18, including one of his own, occurring on the arm in association with a nævocarcinoma. From personal communications with Dr. Hartzell we learn that he strongly favors the primary origin of Paget's disease and controverts the assertions of Jacobaeus and others as to its secondary nature.

Surgeons in this country who have expressed their views comparatively recently on this subject include J. B. Murphy and Wm. L. Rodman, both of whom look on Paget's disease as a secondary condition, the former, Murphy, frankly siding with Jacobæus and his school in stating that the skin changes arise in primary duct cancer in response to an irritating discharge from the milk ducts, causing irritation and subsequent ulceration of the nipple, and he calls it Paget's cancer instead of Paget's disease. We have already given Hartzell's present views. Stelwagon informs us in a personal communication that like Hartzell he is a firm adherent of the primary and distinctly independent nature of Paget's disease as is Sequeira, and Knowles takes the same view, while Ormsby states that the connection between it and malignant breast disease is not settled but that most authorities look on Paget's disease as benign and precancerous. He has had three cases extramammary in location.

Pathology.—The descriptions of the pathological changes found in Paget's disease have almost without exception been uniform in character. The differences in opinion consist in various views as to the cause and origin of the affection rather than in the histologic manifestations of the disease. The characteristic changes described when it occurs in its common site comprise alterations in the skin and corium, and what are probably secondary changes in the milk ducts and glands of the breast, and of these the greatest interest and speculation have centred in the peculiar appearance of the epiderm, and the question as to its primary or secondary occurrence.

The changes consist in a thickening of the skin caused largely by proliferation and growth downward of the rete mucosum, the cells of which, however, do not exhibit invasive tendencies, a fact particularly emphasized by practically all writers on the subject. The interpapillary bodies themselves are thickened and present a rounded appearance and in some cases encroach upon the papillæ to such an extent that they are almost obliterated. The epithelial cells in this layer are the seat of the changes which give to the disease its peculiar

character. Beginning probably in the prickle-cells, and extending gradually to the basal and then to the more superficial cells, the disease produces a peculiar swelling and vacuolation. The cells are greatly increased in size, the protoplasm is clear or finely granular, and the nuclei are large, vesicular and show many irregular mitotic figures. As the process advances almost the entire thickness of the epiderm becomes involved, and only an occasionally normal cell is seen. The degeneration of the prickle-cells becomes so complete that their characteristics are lost. Keratin formation, intercellular spines, and fibrillation cannot be demonstrated in the cells which have undergone vacuolation. This fact has been used by some writers to indicate that the Paget cells are not derivatives of the epiderm. It seems more rational, however, in view of their regular distribution in the rete, and in the absence of characteristics of gland epithelium, to assume an alteration in the cell characteristics by which they lose their innate peculiarities, than to explain their presence by a process of metastasis unlike that observed in any other form of breast cancer. The superficial layer of squamous cells is frequently preserved in certain areas, and shows the usual characteristics of keratinization. Unna describes other forms of cells in which the appearances are modified by resistance of the hardened outer layer, as in the upper layers of the rete, also the changes due to compression of neighboring cells, development of " encysted " cells, etc. In more advanced stages of the disease ulceration results in a disappearance of the epiderm, so that the inflammatory tissue produced in the corium is exposed and forms the base of the ulcer. The edges of the lesion exhibit in sections under the microscope an abrupt change from the normal to the diseased epiderm.

The inflammatory reaction, or as some believe the initial manifestation of Paget's disease, consists in an intense cellular collection which appears under the epithelial layer in the corium, or to a lesser extent about the ducts and acini, which subsequently undergo proliferation of their epithelial cells. The infiltration for the most part consists of round cells, although many plasma cells and a lesser number of connective tissue cells and leucocytes are noted. Unna speaks of this as a pure plasmoma which acts as a bulwark. The zone of reaction seems to vary in accordance with the skin changes. We have noticed the most intense reaction in those cases in which Paget's disease is most advanced, and, when ulceration arises, the cellular infiltration reaches its maximum. It too is sharply bounded by the edge of the lesion. Many new blood-vessels with thin walls and resembling those found in granula-

tion tissue are met with, in fact the entire process has been likened to that seen in a granulating wound.

The superficial milk ducts contain a large number of cells in a stage of active proliferation, and in some instances the duct becomes filled with epithelium. Occlusion most likely occurs near the nipple, for cyst formation is frequently seen, the dilated duct being filled with debris, degenerated epithelial cells and fat droplets. The epithelium itself shows the changes occurring in any actively proliferating process. Some writers have described changes similar to those noted in the skin, and have traced a transition from one cell to another. In our cases we have encountered cells with clear protoplasm and presenting an appearance somewhat resembling the Paget cell, but it must be remembered, however, in many breast tumors both benign and malignant, large, clear, apparently vacuolated cells are met with and that these conditions are regarded as evidence of an active epithelial hyperplasia. The transition between the so-called Paget cells of the skin and the cells in the ducts or in the cancer has been traced by a few writers. The majority of observers have not noted such transition forms. In other cases, and particularly in extramammary Paget's disease, the extension of the process from the skin to the lining cells of the ducts, glands or follicles has been observed. In serial sections we have been able in one case to trace the ducts to their point of opening, at which site the superficial epithelium has been the seat of Paget's disease, but transition forms or the extension of Paget cells from the skin to the ducts could not be demonstrated. Finally the epithelial hyperplasia becomes so active in the smaller ducts and acini that the cells break through the wall and infiltrate the breast stroma as a malignant tumor. As pointed out by Duhring, this process usually is met with in the ducts one or one and one-half inches from the nipple, a fact which we were able to corroborate in two of our cases.

The malignant tumor, which develops in the majority of cases, springs from the epithelium of the ducts, less frequently from that of the acini, and rarely from the cells of the epiderm. There are undoubted examples of Paget's disease in which this latter type of degeneration has occurred, resulting in a squamous-cell carcinoma, and this fact in itself supports the opinion that the disease is not primarily a duct cancer, but a precancerous condition. The carcinoma originating in gland or duct epithelium resembles the type usually encountered in the breast, viz., adenocarcinoma or scirrhous carcinoma. These and other pathological characteristics are described in the studies of our cases which are appended and, with the interpretations which are

placed upon them by other authors, are included in the review of the literature.

When we come to consider the arguments for and against the primary nature of Paget's disease, we find, as mentioned elsewhere, a great divergence of views. Many surgical authorities have been converted to the view that it is a secondary process by the articles of Jacobaeus, Schambacher and Ribbert, which are in effect a return to the views held by Thin. The reasons for this view are based primarily upon the very frequent association of breast cancer with Paget's disease when it comes to histological examination. Also, the superficial changes in the milk ducts, and the apparent connection of these with the diseased areas in the epiderm, and the changed appearance of the cells occupying the rete from that of the prickle-cells, which give them to some observers a resemblance to cancer cells and the cells in the lactiferous ducts, and which lead these observers to identify them as metastases. Other writers, who also uphold the view of the secondary nature of Paget's disease, regard the œdematous cells in this region as prickle-cells which have lost their characteristics by reason of the irritating discharge from the milk ducts, or by reason of diosmosis and osmosis from prolonged contact with the secretions bathing the ulcerated surface. These writers sharply distinguish between cancer cells and Paget cells. Jacobaeus claims in one case to have recognized cells identical with Paget's cells in ulcerating scirrhus, where carcinoma cells substituted the epithelial cells.

As against their views and supporting the conception of Paget's disease as an independent and more or less unique skin disorder is a mass of clinical and pathological evidence which the above-mentioned authors disregard or misinterpret. Cancer of the breast is common while Paget's disease is rare. Speese has examined 450 cases of breast tumor in the University Hospital service of which 2 were Paget's. Oldekop had 3 in 250 cases, and Guleke 7 cases in 782 breast tumors. The common testimony of surgeons of large experience is that they have seen not more than one or two cases. Paget's disease may, and often does, exist on the breast for many years. Such is not the history of malignant disease of a glandular type. There are cases on record in which no cancer in the parenchyma has developed after many years. There are cases in which squamous carcinoma has developed from long standing Paget's disease and then pursued its characteristic course. Paget's disease develops in many other regions, and while it occurs by preference on areas rich in surface glands, it arises and pursues its usual course on such regions as the buttock, the nose,

the neck and the axilla. As regards the histological appearance, it does not resemble that found in any region where an underlying carcinoma frankly ulcerates through the skin. We could not confirm Jacobæus's unsupported observation in this respect, after study of a large series of ulcerating cancers of the breast and other organs. We agree with those authors who find no resemblance between Paget's cells and cancer cells; nor have we been able to trace transitional forms from the cancer cell to the Paget cell. The absence of a direct invasion downward of the corium by the Paget cells is against its being of a malignant or metastatic nature. The development of squamous carcinoma in this and other locations is another argument against its secondary nature and strongly in favor of its classification as a precancerous lesion wherever it arises. We believe that the key to the solution of the problem as to whether the disease is primary and spreads from above downward or secondary and proceeds from below upward, is provided by the study of cases occurring elsewhere than the breast, where the question of irritating discharges and metastases from deep glandular cancers can be eliminated. It is significant that dermatologists who have had almost a monopoly of such cases, while they may differ among themselves as to whether Paget's disease is in itself precancerous or malignant, are almost a unit in regarding it as a primary lesion.

Treatment.—Little need be said as to the treatment except that which is summed up in the words "radical operation." The presence of malignant disease has been shown in the great majority of cases, and the impossibility of predicting its absence in any case. Tumor is absent in many cases clinically in which the microscope shows that infiltration has already occurred. These facts need only to be mentioned to indicate the importance of an early and complete operation. The treatment by X-ray has been disappointing in that, while the superficial lesion may be healed, the deeper malignant process in the breast progresses. The X-ray has proved of great benefit in some extramammary cases, where the location or the extent of the affection did not permit of its radical extirpation.

CONCLUSIONS

1. Paget's disease of the nipple is a primary affection beginning in the cells of the rete Malpighii, potentially malignant, although lacking the ordinary characteristics of malignant disease.

2. It is identical with the disease known under the name of Paget occurring in other regions.

3. It is commonly, although not invariably, followed by glandular carcinoma in the underlying breast tissue.

4. It is precancerous in the sense that it induces epithelial changes in the superficial milk ducts and acini, which are followed by carcinoma. Occasionally, although rarely, it is followed by squamous cell carcinoma of the nipple.

5. The disease is characterized by œdema and vacuolization of the prickle-cells, thickening of the rete, and active mitosis, also by an inflammatory reaction in the corium and a secondary hyperplasia in the milk ducts.

6. It is sharply differentiated from true eczema and scirrhous carcinoma ulcerating at the nipple, and should not be confused with superficial metastases of diffuse cancer situated near the skin.

7. The resulting tumors of the breast and the regional metastases resemble the type of breast cancer usually encountered. When the tumor originates in the skin, it infiltrates and metastasizes in the form of squamous carcinoma.

8. The common association of cancer in the breast with Paget's disease demands as the treatment for Paget's disease the radical operation which is practised in breast cancers in general.

The histories of the cases of Paget's disease studied by us are appended. Also a case of one type of ulcerating scirrhus which simulates it.

Case I.—S. F. (Presbyterian Hospital, January 7, 1915, Dr. J. H. Jopson), aged sixty-seven, no history of neoplasm in family, mother of 3 children, mastitis in right breast during lactation. Present trouble began seven months ago in left breast when she noticed a little sore on nipple which dried up at first when powder was applied. Later no healing possible and would bleed.

Physical Examination.—Elderly female, rather well preserved for her age. General physical examination negative. Left nipple twice as large as opposite, due to ulceration; nipple inverted, ulceration ⅞ by ¾ of inch, shallow crater formed by erosion in centre. The areola is healthy, no underlying induration in breast. No palpable axillary nodes. Ulceration epitheliomatous in appearance, pink in color, covered here and there with islands of new-formed bluish-white epithelium. There is a constant exudation of serum. No pain or burning; two small capillary nævi on breast (Fig. 1).

Operation.—Complete Halstead; no enlarged axillary nodes found.

FIG. 1. FIG. 2.

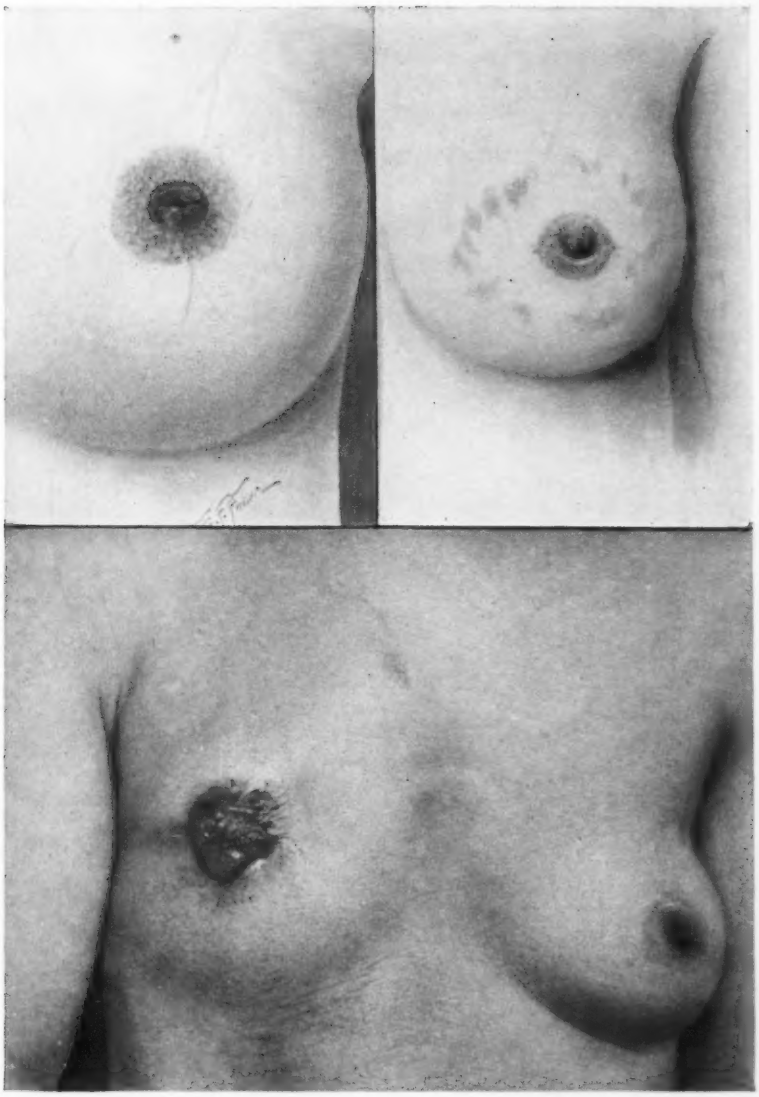

FIG. 3.

FIG. 1.—Paget's disease of the nipple.
FIG. 2.—Diffuse scirrhus of the breast simulating Paget's disease.
FIG. 3.—Ulcerating scirrhus involving the nipple (Rodman).

Pathologic Examination.—5781. Specimen consists of a breast, pectoral muscle and axillary lymphatics. The nipple is slightly inverted, bright red in color and presents a superficial ulceration which is covered by several minute whitish areas resembling epithelium. The skin overlying the breast is normal. The areola is slightly pigmented and two small capillary nævi are noted on the surface some little distance from the nipple. Section through the central portion of the breast shows that the tissue immediately beneath the nipple is denser than normal but does not contain any of the gross evidences of malignant degeneration. The breast elsewhere shows a moderate degree of fibrosis occurring in the midst of a diffuse fatty overgrowth. In a few places this fibrous overgrowth is very dense and occurs in the form of small round nodules. The axillary lymphatics contain a few enlarged lymph-nodes which are apparently normal.

Microscopic Examination.—Sections taken through the nipple and the tissues beneath show a stratified squamous lining covering the skin and the nipple; this is normal for the most part but as the region of the nipple is approached the character of the epithelium changes. The epithelial lining suddenly becomes thicker, the interpapillary bodies decidedly broader than normal and extend deeper into the corium than the adjacent normal ones. The most pronounced changes are encountered in the epithelial cells. These throughout the entire extent of the epidermis are enlarged, clear and vacuolated in appearance (Fig. 5). The nuceli of the cells are enlarged and swollen and in many, irregular mitotic figures are to be seen. The condition of vacuolation has resulted in a disappearance of the intercellular spines in many of the cells; they are to be seen in some in the more superficial portion of the skin and particularly where the condition of vacuolation is less marked. While the entire thickness of the skin in some places is the seat of this condition (vacuolation), in other areas only the basal cells are involved and here keratinization of the overlying epithelium is well marked. Immediately beneath the skin is an inflammatory reaction which extends through the corium but only where it is covered by epiderm the seat of Paget's disease. In those situations in which a normal area of epiderm is encountered the subepithelial inflammatory reaction abruptly ceases to exist. The reaction consists of newly-formed blood-vessels with thin walls, surrounded with leucocytes, plasma cells and spindle connective tissue cells.

The sections taken through the milk ducts immediately beneath the nipple show several which are normal and others which are markedly altered in appearance (Figs. 6 and 7). In the latter the epithelial lining has become heaped up so that in some instances the duct seems almost solid in appearance. In others the hyperplastic epithelium has caused an appreciable increase in the calibre of the duct and widening of the lumen. The epithelium is columnar, the cells contain granular protoplasm and the nuclei show many mitotic figures. In some instances the ducts can be traced directly to the opening in the nipple. Here the superficial epithelium is the seat of Paget's disease, but typical Paget's cells do not extend into the mouth of the duct nor does the epithelium lining the duct take on the characteristic changes of Paget's disease. About the ducts the seat of the most intense epithelial hyperplasia and to a less extent about the acini, an inflammatory

reaction similar to that beneath the skin is encountered. The changes described are found in the ducts immediately beneath the nipple, there is no tendency toward a breaking through of the elastic membrane of the duct. The epithelial hyperplasia extends to the ducts situated 3 and 4 cm. beneath the nipple. Many of these are dilated, forming cysts containing a homogeneous structureless material and fat droplets. The epithelial lining in these cysts in some places has disappeared apparently by pressure atrophy, and in others is low and flat in appearance. In many of the ducts in this situation (3 cm. from the nipple) the epithelial proliferation is no longer confined to the duct itself and outgrowths of solid plugs of epithelium are formed in the surrounding tissues. The first evidence of malignant infiltration is noted in a duct situated 1 cm. from the nipple, the change is much more pronounced, however, in the ducts and acini situated deeper in the breast. In the surrounding breast tissue there is no evidence of malignant degeneration, but the glands are numerous and contain proliferating epithelium such as is encountered in the adenomatous type of chronic cystic mastitis. The lymph-nodes were unchanged.

Summary.—The changes found in the skin are characteristic of Paget's disease. The inflammatory reaction, the hyperplasia within the ducts and the final malignant degeneration correspond to the series of changes seen in other cases. The case is noteworthy in that the connection between the superficial skin changes at the point of opening of one of the ducts could be traced. In this situation there is no indication of a substitution or metastasis of the hyperplastic duct epithelium into the epidermis as has been suggested by many writers, and, on the other hand, the Paget cells in the epidermis are not found in the ducts or in the acini. The case confirms the view that Paget's disease begins in and is limited to the epidermis, and that the cancer is secondary and is induced by the primary disease of the skin which in some unknown manner prepares the ground for a malignant degeneration.

CASE II.—Mrs. J. S., aged fifty, patient of Dr. C. H. Frazier. The patient is the mother of four children. There is no history of a neoplasm in the family. She was admitted and operated on for an umbilical hernia. During her convalescence she complained of pain in the left breast, when an examination revealed a reddened condition about the nipple. The surface was covered with scales and was constantly bathed in a thin watery secretion.

Amputation of the breast was performed and was followed by recurrence in two years for which several other operations were performed, death resulting four years after the first operation from extensive metastasis.

Pathologic Examination.—2410. Specimen consists of a breast with underlying pectoral muscle and axillary lymphatics. The skin surrounding the nipple is red, covered with crusts, not infiltrated, the nipple is not retracted. The area of dermatitis is circular in outline and about two inches in diameter. Cross-section through the breast, including the nipple, shows a fibrous overgrowth but no distinct tumor formation immediately beneath

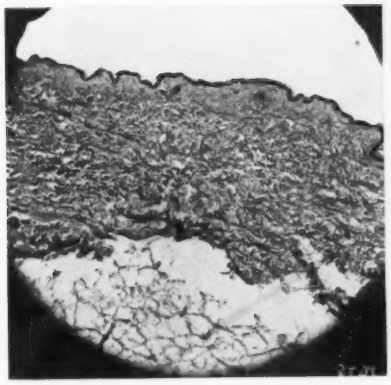

FIG. 4.—Histological appearance in case of diffuse scirrhus shown in Fig. 2. Normal skin and emboli of cancer cells in lymphatics.

FIG. 5.—Case I. High power photomicrograph of the skin, showing vacuolation and mitoses of cells in the prickle layer.

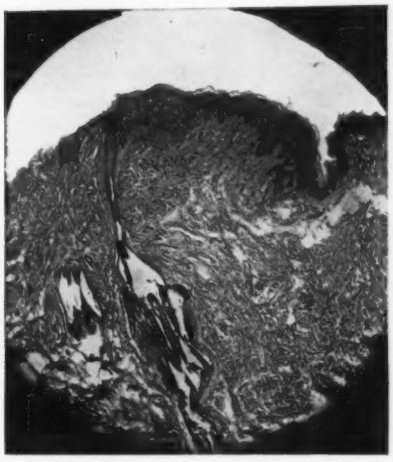

FIG. 6.—The squamous epithelium of the skin is the seat of Paget's disease, there is no involvement of the duct epithelium.

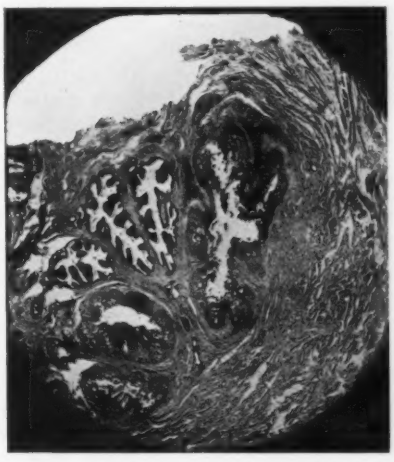

FIG. 7.—Dilatation of milk ducts and hyperplasia of the lining epithelium with a tendency toward infiltration of the stroma.

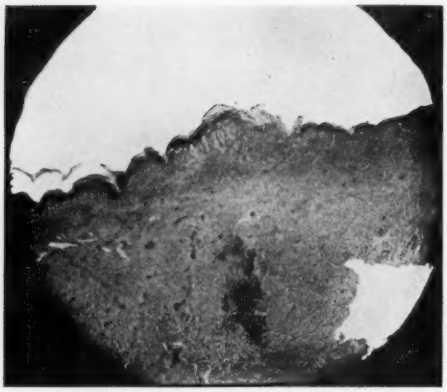

FIG. 8.—Case II. The entire epiderm is involved, the cells enlarged and vacuolated.

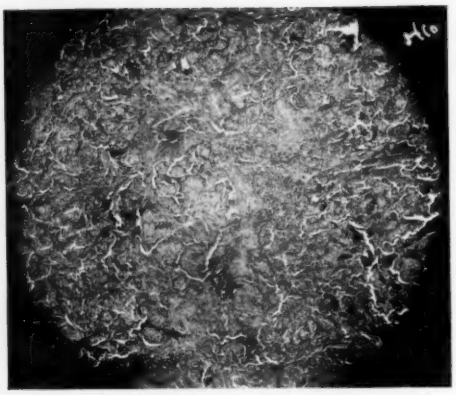

FIG. 9.—Section from the tumor.

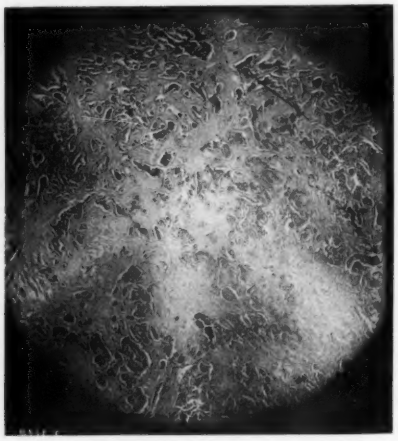

FIG. 10.—Metastasis to axillary lymph-nodes.

FIG. 11. — The epiderm under high power, showing characteristic vacuolation of cells.

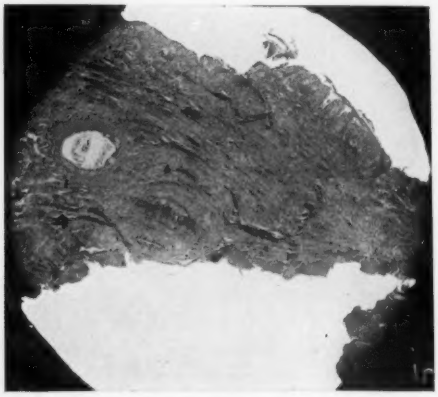

FIG. 12.—Case III. Vacuolation of the cells indistinctly seen. Slight dilatation of ducts present, but no infiltration of epithelium into stroma.

FIG. 13.—Case VI. Section through nipple in an ulcerating scirrhus. The squamous epithelium is unchanged, the underlying tissues infiltrated with cancer.

the nipple. In the upper and outer quadrant of the breast is a hard nodular mass 3 cm. in diameter which on section is dense and white in color. The surrounding areas of breast tissue show slight fibrous overgrowth. In the axilla several enlarged lymph-nodes are present, and possess the same characteristics as the hard tumor already described.

Microscopic Examination (Figs. 8, 9, 10 and 11).—Section of the skin taken from the region of the nipple shows the greater portion of the epidermis to be transformed by a process which has caused pronounced vacuolation of the cells. The greatly enlarged cells are clear or slightly granular in appearance, the nuclei vesicular and exhibiting many mitotic figures. In a few areas intact portions of epidermis appear between areas the seat of these changes, and in these situations the line of demarcation is fairly sharp and only a few of the basal cells are vacuolated. The cells immediately above appear unaltered and intercellular spines are demonstrated in the prickle layer. In the epidermis the seat of the most pronounced transformation, all the cells are similarly changed and there is no distinction between the cells until the superficial layer is encountered where keratinization is noted. In the corium is a diffuse reaction consisting of leucocytes, plasma cells and many capillaries. The enlargement and swelling of the interpapillary processes has resulted in the occlusion and compression of the papillæ and in a few places has caused an apparent cutting off of the papillæ so that they seem to be included in the skin. In the tissues beneath the nipple, a moderate dilatation of the ducts and hyperplasia of the lining cells are met with. The opening of the ducts at the nipple could not be demonstrated. The adjacent tissues contain large numbers of acini surrounded by round cells but no evidence of malignant infiltration. The nodule in the upper and outer quadrant of the breast shows a definite carcinomatous process. Many acini, lined with cuboidal epithelium and altered in shape by reason of pressure of the fibrous stroma, are present. In other areas the tendency toward acinar formation is lost, and here the cells exist as small clusters containing a clear, almost transparent, protoplasm and deeply staining nuclei. In the fibrous stroma a round cell reaction is noted. The axillary lymph-nodes contain cells resembling those found in the breast tumor, the condition representing a metastasis.

Summary.—The case is to be regarded as Paget's disease of the nipple, with secondary carcinoma of the breast. The epithelial hyperplasia in the ducts resembles that observed in other instances. The case is of interest in that the carcinoma developed some distance from the nipple and ducts, contrary to most of the other cases observed by us, in which the superficial ducts or acini showed malignant degeneration.

CASE III.—Case of Dr. George M. Laws. Mrs. G., sixty-three, stated that the right nipple had always been smaller than the left, had been divided into two parts by a shallow cleft since birth and was always sensitive. The family history was negative as regards malignancy. She was the mother of four children and nursed three of them. In February, 1911, she noticed a little moisture in the centre of the cleft. Two months later a tiny scale formed, the latter condition becoming progressively larger. In

January, 1912, the cleft had widened, the nipple became flattened and ulcerated. This condition persisted until the time of examination, November 25, 1912, or twenty-one months after the beginning of the disease. The nipple was found to be entirely absent, there was a shallow ulcer 2 cm. in diameter with reddened edges, although the surrounding skin was normal. There was a chain of pea-sized nodes along the border of the pectoral muscle. The breast elsewhere presented no distinct pathological changes. The ulcer and the surrounding skin were removed under local anæsthesia, and upon the report of Paget's disease radical operation was performed. There had been no recurrence or other disturbance when the patient was last seen, May 4, 1915.

Pathological Examination.—4371. The specimen consists of a shallow ulcer measuring 2 cm. in diameter and 0.5 cm. in thickness; it is surrounded by an area of skin which presents no gross pathological features. The subcutaneous fat is unaltered.

Microscopic examination shows remnants of the epidermis, which for the most part has disappeared and its place is occupied by a mass of inflammatory tissue. The latter is represented by large numbers of leucocytes, plasma cells and newly formed blood-vessels and extends a short distance into the subcutaneous tissues and parallel to the entire surface of the skin ulceration. In the sections in which the epiderm is preserved it is found to be the seat of noteworthy changes. The cells of the basal layer, and to a much less extent in the superficial layers, present a condition of marked vacuolation, the cells being in some cases 2 or 3 times the size of the ordinary cell. The nucleus in some instances has disappeared, in others it is enlarged and irregular in appearance, in other cells mitotic figures are present. While some of the cells are clear the protoplasm in others has a granular appearance. Where the vacuolated condition is well marked a thin outline denotes the cell limits and intercellular spines cannot be determined, these appear, however, in the more superficial layers of the epidermis. In the subcutaneous tissues a downgrowth of epithelium from the epiderm or an infiltration of epithelium from other sources cannot be demonstrated (Fig. 12). In one area one of the superficial milk ducts is encountered, it is surrounded by an intense round cell infiltration resembling that seen in the skin. The epithelium in the duct is hyperplastic and has undergone desquamation so that the duct is partially filled with cells, a few of which contain clear protoplasm and resemble somewhat the Paget cells of the epiderm. The elastic tissue surrounding the ducts is preserved and the proliferative epithelium has not infiltrated the surrounding tissues. An occasional acinus is seen, the epithelial lining has undergone proliferation but the surrounding tissue does not contain as intense an inflammatory reaction as was noted in that surrounding the ducts. The examination of the breast tissue removed at the second operation and the lymph-nodes does not show any changes suggestive of those already described. The breast is the seat of involution, the epithelium in the region adjacent to the nipple is normal.

The histological study shows the characteristics of Paget's disease with the usual changes in the skin epithelium accompanied by an inflammatory reaction beneath. The surrounding breast tissue shows no evidence of malignancy; diagnosis therefore is that of Paget's disease which has not produced a definite carcinomatous process, but has provoked proliferation in the duct epithelium which in time would probably become malignant.

CASE IV.—This case was submitted for study by Dr. William C. Clarke. S. S., aged fifty-three, had a lactation mastitis some years before the development of an eczema about the nipple which persisted for two years until the nipple was destroyed. There was an indefinite mass situated in the upper and outer quadrant of the breast. An area around the nipple was red and weeping without any significant loss of tissue. There were also several small cracks and the surface was covered with scales. This condition alternately dried up, then became fissured and bleeding. A mass was noted in the breast three weeks before operation, but could not be demonstrated in the gross specimen.

Microscopic examination (2441) of a section taken through the area of involved skin and extending well into the underlying tissues shows considerable thickening of the epidermis. The interpapillary processes are elongated and broadened. The epithelium shows numerous enlarged and vacuolated cells, the protoplasm of which for the most part is granular although in some places it is clear. The nuclei are enlarged and swollen in appearance and contain numerous mitotic figures. In the corium a very extensive inflammatory reaction is seen; this is associated with the formation of many new blood-vessels. The round cells extend into the papillæ and into the epiderm itself. Evidences of epithelial hyperplasia are found in the ducts but not to the excessive degree noted in our other cases. A moderate cellular reaction appears about the ducts. Evidences of malignant degeneration are encountered in an area just beneath the skin and extending for a considerable distance into the dense fibrous stroma of the breast, the process apparently extending from below upward. The epithelium just above the area of malignant degeneration has disappeared and its place is occupied by a mass of inflammatory granulation tissue; the epithelium in the vicinity does not show the picture of Paget's disease.

The case represents Paget's disease with the usual changes in the skin, corium and ducts. It appears that the superficial ulceration is caused by the extension of the malignant area upward rather than to the action of the Paget's disease.

CASE V.—Specimen was sent for study by Dr. William C. Clarke. The only available history stated that the breast was removed with the overlying skin and that some superficial excoriations existed for at least two inches about an atrophic nipple. The glandular tissue of the breast was atrophic and largely replaced by fat.

Microscopic examination (447) of the skin in the region of the excoriation shows areas of intact epidermis which abruptly undergo the characteristic changes of Paget's disease. This transformation consists of vacuolation of all the cells of the epidermis with a relative widening and slight dipping down of the interpapillary bodies; and an infiltration of leucocytes, plasma cells and the formation of many new blood-vessels in the corium. In many areas the epidermis has disappeared, so that the granulation tissue described, covered with a narrow zone of necrotic tissue, is exposed. The zone of inflammation is more extensive than in most of the cases studied. It extends deeper into the underlying tissues and to a slight extent beneath the sound skin. The intense reaction is probably due to the extensive loss of epiderm. The epithelial proliferation is pronounced in the superficial ducts and in the acini. In both the ducts and acini solid plugs caused by this hyperplasia are encountered, but a breaking through of the elastic membrane surrounding the ducts does not appear until the ducts situated about 3 cm. from the skin are examined. In this region a carcinomatous process becomes well marked and the fibrous stroma is invaded by atypical acini and irregular aggregations of rather large columnar cells containing large, deeply-staining nuclei and granular protoplasm. Active hyperplasia is indicated by the irregularity in size and shape of the cells and by the presence of numerous mitotic figures.

The case is characterized by the usual picture of Paget's disease which has produced destruction of the skin in some areas. The ducts are the seat of hyperplasia of the lining cells which has produced a definite picture of cancer in a region where the cells have broken through and invaded the stroma.

CASE VI.—E. R., aged fifty-one, a patient of Dr. W. L. Rodman, gave the following history. Five years ago a stabbing pain was noted by the patient in the right breast. This has continued off and on ever since, and in January, 1913, she first observed a small scab. One year previously a reddening to the outside of the right nipple began and the scab followed in the site of the reddened area. There has never been any discharge from the nipple. Two years later the reddened area extended all the way around the nipple, which was slightly eroded and inverted (Fig. 3). The appearance of the breast and the clinical history in many respects suggested Paget's disease. The microscopic findings (1375), however, did not confirm this diagnosis but revealed, in sections made through the nipple, that the process consisted of an infiltration of atypical acini. These grew from below toward the surface and gradually involved the epiderm in which acini can be found (Fig. 13). The changes in the skin represent merely an ulceration secondary to an infiltrating carcinoma and bear no resemblance to the microscopic characteristics of Paget's disease.

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ON EXCISION OF THE TONGUE*

By Astley Paston Cooper Ashhurst, M.D.
of Philadelphia

The purpose of this communication is to call attention to a method of excision of the tongue which may be described as a variant of Crespi and Bastianelli's modification of Langenbeck's operation. Crespi and Bastianelli's Method is not described, so far as I can ascertain, in any of the text-books or systems of surgery at present in use in this country. I have merely mentioned it in my own text-book, and it is also mentioned, without credit to its originators, in Johnson's *Operative Therapeusis,* recently published.

Systematic excision of the tongue goes back to the time of Roux, who is credited[1] with having adopted in 1836 temporary division of the mandible; and who in 1839 did preliminary ligation of the lingual artery, finding then that after dividing the frænum and the anterior pillar of the fauces he could draw the tongue far outside the buccal cavity, and was able to complete the excision of its left half with facility. The method of operation popularized by Whitehead (1881) is a further development of that adopted by Roux.

Sédillot (1844) and Syme (1858) thought to make access easier by temporary division of the symphysis menti, and Kocher has now adopted a slight modification of this operation as his "normal procedure," and prefers it to the lateral suprahyoid operation formerly known by his name. The great advantage which median section of the mandible presents over Whitehead's method is that it permits simultaneous excision of the floor of the mouth when this is necessary. But as the carcinoma usually is situated at the side of the tongue, and spreads toward the fauces and pharynx, this approach gives insufficient access to the seat of disease in the majority of cases, and is best suited to those rather unusual cases where the carcinoma invades the mucosa around the frænum linguæ and does not extend far backward. Moreover, the wound left after operation by Sédillot's or Syme's technic is very prone to infection. In most cases, therefore, it is less applicable than Langenbeck's method (1875), which consists in making an incision

* Read before the American Surgical Association, June 11, 1915.

[1] Demarquay makes this statement; and Verneuil refers to the "Roux-Sédillot Operation."

FIG. 1.—Skin incision for excision of the tongue.

FIG. 2.—The neck dissection has been completed, the cervical lymphatics and fat still attached to skin flap. The neck wound is then tamponed with gauze.

FIG. 3.—The cheek has been turned aside, exposing the tongue. The left anterior pillar of the fauces has been divided, and the scissors are now dividing that on the right.

FIG. 4.—After removal of tongue, floor of mouth is covered partially by suturing mucosa of cheek across alveolus to stump of tongue. A hæmostat is on the right lingual artery in the floor of the mouth.

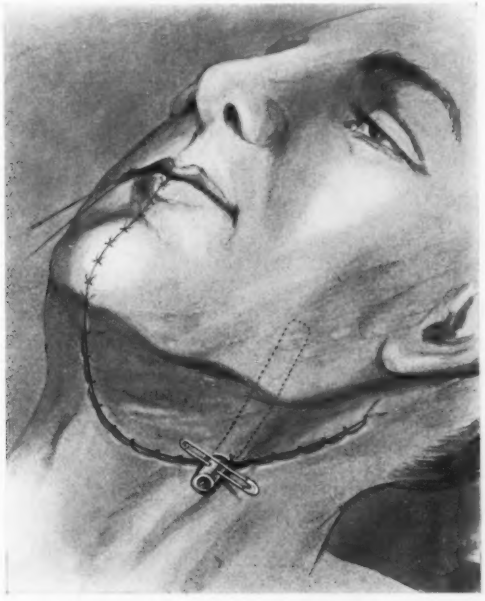


FIG. 5.—Skin incision sutured; drainage tube in place. Suture through glosso-epiglottidean fold retained for first 24 to 36 hours.

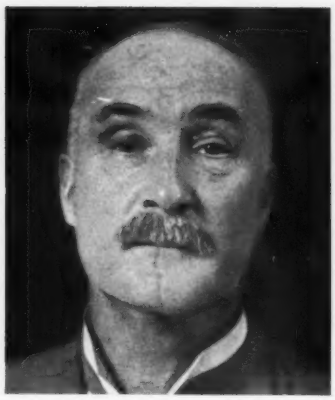


FIG. 6.—Excision of tongue, eight months after operation.

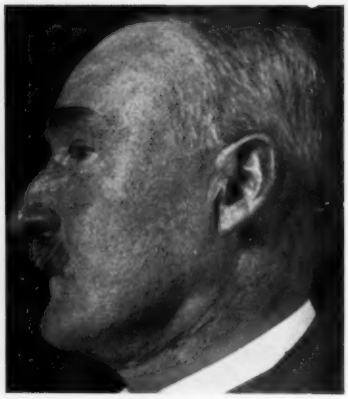
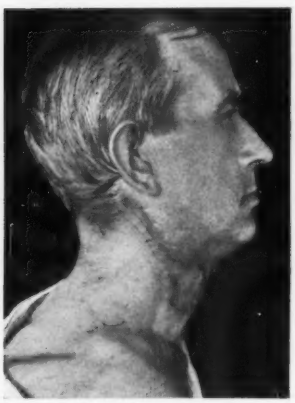
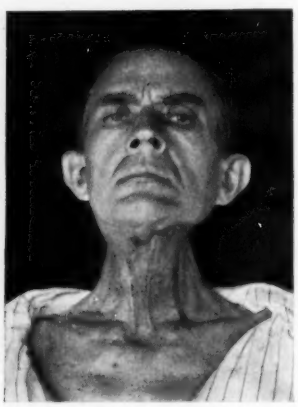


FIG. 7.—Excision of tongue, eight months after operation.





A *B*

FIG. 9.—*A*.' Four weeks after second operation (on right side of neck). *B*. Four weeks after second operation, two months after first operation (on left side of neck).

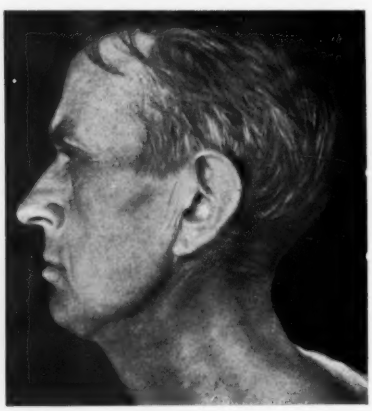


FIG. 10.—Two months after operation.

from the angle of the mouth downward to the level of the thyroid cartilage, with division of the mandible between the first and second molar teeth. The remarkably low immediate mortality which attended this operation in Volkmann's clinic appears to have passed from memory as completely as the operation has from practice. In 1889 Krause reported Volkmann's results with this operation from 1875 to 1888: There were 35 such operations in which temporary resection of the jaw was done, with 2 deaths, a mortality of 5.7 per cent.; and there were 56 similar operations in which the disease was not so far advanced as to make division of the mandible necessary for complete extirpation, with not a single death from the operation; or, combining the two series of operations, there were 91 excisions of the tongue, with only 2 deaths, a mortality of 2.2 per cent., which compares favorably with much more modern statistics.

There are, however, two great objections to Langenbeck's method. The first is the unsightly scar, and the division of the branches of the facial nerve which the skin incision involves; the other, and a weightier objection, is that no adequate provision is made for extirpation of the involved lymph-nodes. In Crespi and Bastianelli's modification (1889) of Langenbeck's operation the former objection is absent, as the skin incision divides the lower lip in the midline and is continued outward along the body of the jaw to its angle and thence to the anterior border of the sternomastoid; but the second objection, the inadequacy of the exposure for extirpation of the lymphatics, still holds. They describe their method thus:

The soft parts are incised from the midline of the lower lip to the symphysis menti, and the incision is then prolonged outward along the lower border of the mandible to the anterior border of the sternomastoid. (In one case of invasion of the lateral wall of the pharynx, this incision was prolonged downward along the anterior border of the sternomastoid.)

This incision passes to bone through the lower lip and as far as the insertion of the masseter, and through the soft parts posteriorly as deep as necessary to allow the flap to be turned up well. This flap, composed of lower lip and cheek, is then turned upward. As the skin retracts downward, this exposes the submaxillary fossa, and the submaxillary salivary gland and lymph-nodes can now be extirpated, and the lingual and facial arteries and their veins ligated. By virtue of the prolongation of the incision along the sternomastoid it is possible to expose the great vessels and to draw them out of harm's way by a retractor.

Then the mandible is divided. The best point is in front of the next to last molar tooth. The mandible is sawed obliquely, as recommended by Langenbeck, from behind outward and forward. The fragments now separate by muscular tension, and are pulled widely asunder, securing "enormous" space. Then it remains to remove the tumor, according to the individual case.

The mandible is sutured, and the flap (lower lip and cheek) is replaced and accurately sutured, with adequate provision for drainage.

In a later publication (1902) Bastianelli further extended this procedure, as follows:

By the incision represented in Fig. 8*A*, he sought methodically the ablation of the lymphatics, even if they were apparently healthy, in all cases of lingual cancer, if the strength of the patient permitted.

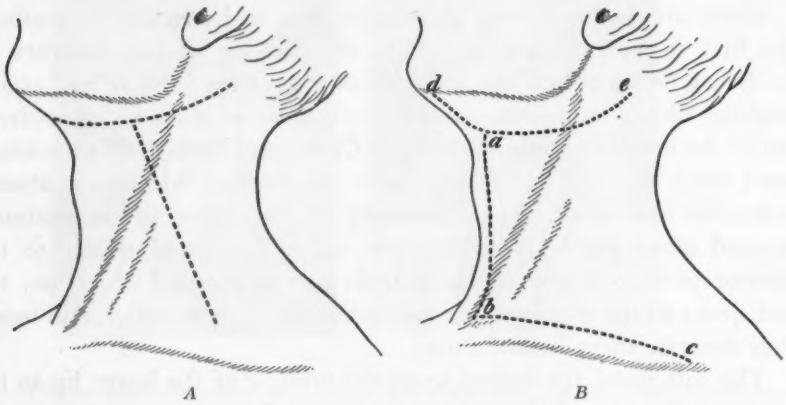


FIG. 8.—*A*. Bastianelli's incisions for extirpation of the cervical lymphatics. *B*. Incisions suggested by writer.

A. *Neck Part of the Operation.*—1. First he makes a semilunar incision, with convexity below, from the symphysis menti along the midline to the hyoid bone, and then outward along its greater cornu, joining the anterior margin of the sternomastoid, and if necessary prolonged backward toward the nucha. The skin and connective tissue and platysma are incised, the external jugular vein is divided between two ligatures, and the flap is raised and fixed to the cheek by a suture. Then to clear the submental and submaxillary regions thoroughly the first step is to isolate and *ligate the external carotid artery* between the superior thyroid and lingual, or even just above the bifurcation. The venous branches must all be ligated doubly and cut between. Everything being cleared up to the mandible, the facial artery and

vein are ligated here, and then the mass is removed. The branch of the facial nerve to the muscles of the lower lip is injured, but, as he points out, this is true of all operations.

2. Hæmostasis being complete, the wound is tamponed, and one proceeds to the removal of the deep upper carotid glands and inferior cervical glands. The former are often invaded, and if they make a tumor it may be possible to remove them through the incision already made, dissecting them from the sternomastoid and perhaps from the pharyngeal wall, taking care to avoid injury to the superior laryngeal nerve. If they do not make a tumor, and are little enlarged and scattered, or if apparently healthy, it is necessary to use an additional incision to expose them. This *second incision* is made perpendicular to the first which it leaves at the anterior border of the sternomastoid, about the level of the hyoid bone, and passes obliquely back and out to the supraclavicular fossa (Fig. 8*A*). In fact this incision runs almost parallel to the omohyoid muscle and a little higher. It may be necessary to cut the sternomastoid across to facilitate exposure, turning its ends up and down and leaving its deep surface if necessary attached to the glandular mass. It may even be necessary to excise the muscle for a certain extent. He adopted section of the sternomastoid as a rule. The spinal accessory nerve is preserved. The dissection is difficult if there is no tumor mass, and numerous ligatures are required. The external jugular vein may be cut between two ligatures. The transverse scapular artery may be preserved. The cutaneous supraclavicular nerves are always cut, and the great vessels, the vagus and sympathetic nerves laid bare. The internal jugular vein may be resected with the glands if adherent. It is very important always to ligate or clamp above the tumor mass before cutting it out (to guard against recurrent bleeding). "The operation up to this stage always takes over one hour, good assistance, and patience."

If the other side of the neck is possibly involved, it is not operated on until the first side has healed. When the first side of the neck is completed, the wound is tamponed, and the second part of the operation (excision of the tongue) is undertaken immediately if the general condition of the patient permits; if not, it is postponed for eight to ten days. If a two-stage operation is necessary it is better to do the neck operation before that on the tongue; because, he says, after removal of the tongue there must elapse many days, sometimes ***months,*** before the patient can stand a second operation.

B. *Tongue Part of the Operation.*—1. If the lesion is limited to the anterior part of the tongue up to the pillar of the palate, or even if

extensive but the tongue still mobile, one succeeds well by the intrabuccal method.

2. If the tumor, even if not diffuse, extends deeply toward the floor of the mouth, any intrabuccal operation is futile.

(*a*) If the tumor is mobile, even in part, Bastianelli follows Kocher's lateral suprahyoid method.

(*b*) If the tumor is diffuse, but not posteriorly, he adopts median division of the mandible.

(*c*) If the tongue is fixed and the tumor extends posteriorly, he adopts systematically division of the mandible near the next to last molar (turning the cheek aside as in Crespi and Bastianelli's method already described).

At the end of the operation Bastianelli sutures the inside of the mouth as well as possible, and then packs the mouth with iodoform gauze. The skin is sutured only at its three extremities: (1) in the midline, (2) at the posterior angle, and (3) below; thus leaving a great central opening which is packed with gauze to avoid secondary infection of the neck wound which he regards otherwise as inevitable.

The slight modification of Crespi and Bastianelli's operation, to which I desire to call attention, was worked out on the cadaver in the Laboratory of Operative Surgery of the University of Pennsylvania. The operation includes removal of the upper cervical and submaxillary lymphatics on the side affected, and of the tongue, at the same sitting. Thus it is designed for cases where the disease is undoubtedly still in the operable stage. As a dissection of this magnitude, when thoroughly done, requires two hours for its performance, very few patients will be in condition to endure a more extensive operation at one sitting. If a more extensive neck operation is required it will be proper in almost every case to divide the operation into two or more sittings. Whenever an operation for excision of the tongue is done in two or more stages, the surgeon should not neglect Bloodgood's sound advice to cauterize the floor of the mouth both from above and from below.

Technic of the Operation.[2]—The patient being anæsthetized[3] and placed in the head-high position, an incision is made from the point of the chin downward in the midline to the hyoid bone, and thence along the side of the neck

[2] The figures illustrating the technic of the operation were drawn by Mr. E. F. Faber from dissections by the writer in the Laboratory of Operative Surgery of the University of Pennsylvania.

[3] Intratracheal insufflation of ether should be used, preceded by thirty minutes by a hypodermic injection of morphine sulphate (one-sixth of a grain) and atropin sulphate (one one-hundredth of a grain).

affected, following the folds of the skin, well below the body of the mandible, to the mastoid (Fig. 1). This incision passes only as deep as the platysma, and is at once undermined beyond the midline in the submental region, and downward toward the root of the neck. When this undermining has been completed, a block dissection of the neck is commenced at the circumference of the area thus exposed. That is to say, the submental region is cleared down to the muscles (digastrics, mylohyoids, sternohyoids) from the far side of the midline toward the diseased side of the neck; and the dissection extends upward from well below the bifurcation of the common carotid artery to the floor of the mouth. As the dissection is carried from below upward the descendens hypoglossi nerve is spared if possible, but all venous branches and the superior thyroid, lingual, and facial arteries are doubly clamped, divided and ligated as they are encountered, thus ensuring the removal of all the lymphatics in one mass. The hypoglossal nerve itself is preserved, as well as the spinal accessory; both of them should be clearly exposed. The superior laryngeal nerve should also be preserved. The dissection is then continued across the mylohyoid and around its posterior border into the floor of the mouth, removing the entire submaxillary salivary gland along with the rest of the cervical tissues. The lower portion of the parotid gland is also cut away to ensure complete removal of lymphatics in this region. The mucosa between the tongue and mandible is not divided at this time, but the entire mass which has been dissected free is turned up with the skin flap upon the patient's cheek (Fig. 2). This mass is then dissected off the skin flap, the platysma being removed with the mass, and the facial artery being ligated on the body of the mandible, to prevent recurrent hemorrhage. The large wound is then swabbed out with a two per cent. alcoholic solution of iodine, and is covered with a hot, moist pack. This terminates the first stage of the operation, which consumes about an hour.

The *second stage* of the operation comprises the removal of the tongue. A stout linen suture is passed through the tip of the tongue, to be used as a tractor, and a mouth-gag is inserted on the opposite side of the mouth. The original skin incision is then continued upward from the point of the chin to the free border of the lip, dividing the lip in the midline. The mucous membrane between the lip and mandible is then divided with scissors, outward until the ascending ramus of the mandible is reached. The masseter is not cut. The cheek is then turned aside. This gives excellent access to the tongue. Another stout line suture is now passed through the glosso-epiglottidean fold, and both this and the suture through the tip of the tongue are drawn taut. Gauze is then packed loosely in the pharynx, around the intratracheal tube. The surgeon next divides the frænum linguæ with scissors, and continues the division of the mucous membrane of the floor of the mouth from this point backward to the anterior pillar of the fauces, first on the opposite, then on the diseased side. The anterior pillars of the fauces are then divided on both sides, and the tongue is drawn well out of the mouth (Fig. 3). The tongue is then severed half way across its base (at least 2 cm. beyond the visible limits of the carcinoma) on the diseased side, and then from the tip of the tongue backward along the floor of the mouth, to the transverse section, also on the diseased side. The bleeding up to this point will be trifling, as the lingual artery on this side has previously been tied at its origin in the neck (before the dorsalis linguæ branch is given off). The tongue is now held in the mouth solely by the hyoglossus and genio-

hyoglossus muscles on the side opposite to that diseased; as these are cut from before backward, the spurting lingual artery of that side is caught in a hæmostat, and if the dorsalis linguæ also spurts it likewise is caught in the stump of the tongue, which is held up in good view by means of the suture previously passed through the glosso-epiglottidean fold. These clamped arteries are ligated. Molar teeth on the diseased side are then extracted and the corresponding alveolus is cleared of mucous membrane; if necessary the alveolus may be excised. This permits the mucosa on the buccal surface of the cheek to be drawn in as a flap and sutured across the denuded alveolus to the stump of the tongue (Fig. 4), thus rendering a bucco-cervical fistula less likely. The remaining portion of the stump of the tongue is sutured as securely as is possible to the mucosa still remaining on the inner surface of the alveolus throughout its extent; and the mucosa of the vestibule of the mouth is sutured to that of the lower lip, from behind forward. A few buried sutures are used to attach the cheek to the body of the jaw, and the skin wound is accurately closed, with rubber tube drainage from below the floor of the mouth to the most dependent portion of the incision (Fig. 5). The pharyngeal gauze and intratracheal tube are then removed, but the suture through the glosso-epiglottidean fold is allowed to remain for twenty-four hours or longer, until the patient regains the power of swallowing.

A man, aged fifty-nine years, was operated on by me, at the Episcopal Hospital, by the method detailed above, on September 25, 1913, the carcinoma having been present for five months or more.[4] He was encouraged to swallow immediately after operation, and slept well the first night after swallowing a dose of paraldehyde. He was able to take liquid nourishment from the first attempt. On the third, fourth and fifth days after operation a little liquid food discharged through the neck wound in swallowing, but this did not recur. He left his bed on the sixth day, and walked out of the hospital on the twelfth day after operation.

The accompanying photographs (Figs. 6 and 7), made eight months after operation, show the excellent cosmetic result. At present, one year and eight months after operation, there is no evidence of recurrence, and the patient is in excellent health.

Excision of All the Cervical Lymphatics.—When removal of all the cervical lypmphatics is contemplated it is advisable to do the excision of the tongue at a second operation, two or three weeks after the neck operation. I believe systematic excision of the sternomastoid and omohyoid muscles in one mass with the involved lymph-nodes facilitates the dissection and renders recurrence less likely. I venture to suggest the following skin incisions for such an operation (Fig. 8).

The incision (*a-b*) begins at the hyoid *near* the midline, and passes straight downward to the suprasternal notch; it is continued thence along the clavicle to the acromion (*b-c*). The triangular flap thus outlined containing only the skin (not the platysma) is raised and the deep dissection is begun at the root of the neck, after section of the sternal and clavicular attachments of the

[4] This case was reported in ANNALS OF SURGERY, 1914, i, 289.

sternomastoid. When more room becomes necessary the incision is extended from *a* to *e*, and this large flap, *containing the skin only*, is reflected toward the trapezius as a base. When in the further course of the dissection the submaxillary and submental regions are reached, and still more room is required, the incision from *a* to *d* is made, and the flap *dae* is turned up over the mandible. In this manner free exposure of the entire side of the neck is secured from clavicle to floor of mouth, and all the diseased structures are removed in one mass, the sternomastoid being sectioned again close to the mastoid. After thorough cauterization (black heat) of the floor of the mouth from beneath the jaw, the flaps are replaced and accurately sutured, with tube drainage at *a* and at *c*.

I had some fear at first that the extensive skin flap *eabc* might slough, but in the two instances in which I have employed this method (Figs. 9 and 10) the flap seemed to act as an immense Wolfe skin graft, and the only sloughing which occurred (insignificant in extent) was at the point *a*.

The object in making the incision *a–b* to one side of the midline is to provide for a similar incision a few weeks later on the other side of the neck; by leaving a small strip of skin in the midline between the two longitudinal incisions, better nutrition is assured the flap on the second side of the neck than if this were to be formed by cutting along the cicatrix of the first operation. As the flaps are well undermined in the submental region at each operation, no lymph-nodes here can escape removal.

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CONSERVATIVE OPERATIONS IN CYSTS OF THE BREAST*

By Frank E. Bunts, M.D.
of Cleveland, Ohio

At the last meeting of this Association the surgical treatment of cysts of the breast received somewhat extended consideration both in the splendid paper presented by Drs. Greenough and Simmons, and in the valuable discussion which that paper evoked. I must confess that the general trend of opinion expressed at that time somewhat startled me, as it was apparently so much at variance with the method which I had ordinarily pursued.

In general, I think, the impression obtained was that since a certain number, variously estimated by different writers, of cases of cysts of the breast were followed by carcinoma, and since women were becoming more keenly alive to the importance of all breast tumors and of their prospective relation to carcinoma, and therefore more willing to submit to extensive operations, the truly conservative treatment was amputation of the entire breast and possibly removal of the axillary contents at the same time.

It is not my purpose to go into a consideration of the various types of cysts of the breast, for it is difficult and often impossible to differentiate them before operation, and even afterwards, in some cases. The position taken by most, was that it was a dangerous matter to simply remove a cyst and then remove the entire breast subsequently if the growth proved upon pathologic examination to be malignant, and therefore the radical operation became the truly conservative one.

I am not aware that it has as yet been definitely established that the cyst is the cause of the cancer, but rather that cancer is present in a certain number of cases in which a cyst has developed. Just as chronic mastitis and the changes in the breast due to non-functionating seem to predispose in a certain number of cases to carcinoma, so do we find that they predispose also to the development of cystic mastitis. We know, too, that a very considerable number of breasts will develop carcinoma without any predisposing cause which we have thus far been able to establish.

It was with these thoughts in mind, and a feeling that the sanction of this Association to the doctrine that cysts of the breast demanded total amputation was fraught with unusual danger and hardship to women if it became the rule of action of those whose clinical experience

* Read before the American Surgical Association, June 10, 1915.

would not allow of making exceptions, that I took up the study of the cases of this disease occurring in the practice of my associates, Drs. Crile and Lower, and myself.

Among a series of 648 operations upon the breast for every kind of disease, there were recorded 68 cases of cysts of the breast, nearly 10 per cent. These 68 represent all types of breast cysts without further classification. Many of them occurred among ward charity patients difficult or impossible to trace, so that we succeeded in getting but 55 replies from letters sent both to patients and attending physicians, and yet the significant fact was, that in not one of the 55 replies was there the history of the subsequent development of cancer. It is true that in 5 cases amputation of both breasts was performed and in 15 amputations of one breast, leaving 48 in which only a partial amputation or excision simply of the cyst was performed. In 13 of the amputations, the pathologic diagnosis of cystadenoma was reported, in 3 multiple cysts, and in 3 simple cysts, without any further explanation, and in 1 cystic papilloma. The same diagnoses were made in many of the cases in which only partial amputation or resection of the cysts was performed, so that there does not appear on the face of the records any special reason for the complete removal as contrasted with the partial removal. In other words, certain clinical symptoms not easily defined, and possibly not always well founded, have determined the more severe and more mutilating operation.

In a general way it has seemed that cases with multiple small cysts or with the symptoms of diffuse general mastitis without palpable cysts were the ones demanding most careful consideration with regard to the question of amputation, while those presenting single or even multiple well-defined cysts were the ones in which amputation was least frequent. Nevertheless it remains true, in my estimation, that each case demands its own consideration, and I believe that the results in this series, at least, justifies this conclusion.

The ages of these 20 cases of total amputation varied from twenty-four to fifty-two years, the average being forty-one years, while in the remaining cases in which only the excision of the cyst was done, the ages varied from twenty to fifty-seven years, the average being slightly over thirty-nine years.

It is perhaps of interest to note the frequency of their occurrence with regard to age; in the decade between twenty and thirty, 10 cases were operated; between thirty and forty, 20 cases; and between forty and fifty, 28 cases, the remainder being above fifty or else the age not recorded.

Very little information can be gained from these figures except that more cases came to operation between forty and fifty years of age, a period commonly accepted as the cancer age, than at any other time, a period when the changes incident to a chronic mastitis may eventuate in carcinoma or cystoma, and it does not necessarily follow by any means that the carcinoma is developed because of the pre-existing cyst, since the other predisposing factors of carcinoma are most apt to be present at this time.

The statements of patients regarding the duration of the lump or cyst are notoriously untrustworthy and in this series of cases the shortest time was one day and the longest eighteen years, and I still have under observation a patient with multiple cysts in both breasts in which operation was refused twenty years ago, and another in which there has been a sanious discharge from the nipple for over six years and yet no other present sign of malignancy exists after this lapse of time.

It is not at all clear in my mind in looking over the record of these 68 cases that marriage or celibacy, child-bearing or non-child-bearing has much to do with the occurrence of cysts of the breast; thus, 48 were married, 18 single, and 2 no record; and of the 48 married patients 15 had children, 13 had not, and in 20 there were no records as to this fact.

In considering the advisability or necessity of operation, it seems to me that we must first of all assume that every female breast is, potentially, a cancer-bearing organ and that their early removal would obviate the occurrence of one of the most dreaded of all diseases, but surely this could not be accepted as an indication for operation. It has been said that after the age of thirty years amputation is the conservative procedure. I confess I am unable to agree with this view. The average ages of two different groups of these cases were forty-one and thirty-nine years respectively, and 48 of them were between thirty and fifty years of age. It certainly would have been a needless sacrifice to have performed a complete operation in these cases. Even with the higher appreciation which many women now have of the dangers that attend the neglect of lumps in their breasts, we should hesitate to promulgate a mode of procedure sanctioned by their fears, but bitterly resented as a mortifying mutilation which they are compelled to accept because medical science has so ruled it. Such a mutilation is no light thing to a woman in the prime of life, though her fear of cancer of the breast may prompt her to ready sacrifice of it.

The final decision as to whether or not a complete operation should be performed should, in my estimation, be determined by the clinical and physical aspects of the tumor and of the breast in which it is found,

and no arbitrary age limit should be adopted as the determining factor. It is true that in some cases of partial resection of the breast after the manner of Warren's operation, carcinoma may subsequently develop, but so it may in any breast, and, until the relation between cysts and carcinoma is more definitely determined from an etiologic stand-point, it seems to me that in a large proportion of cases of cyst of the breast, the partial operation, consisting of the removal of the cyst with a considerable section of the breast tissue containing it, is the preferable operation, and that a carcinoma occurring in that breast subsequently should be dealt with in the same manner as if it were an entirely distinct disease.

AMPUTATION OF THE BREAST BY A TRANSVERSE INCISION

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The operation described below embodies the principles laid down by Halstead, with the following: The axilla is attacked first, in order to determine the extent of the lymphatic involvement and the feasibility of radical treatment (Gross); in order to secure, once for all, at their origin, the blood-vessels supplying the breast, thus minimizing hemorrhage, economizing time, and preventing shock (Meyer); in order to suppress lymphatic drainage as early as possible and prevent neoplastic dissemination (Gerster); and in order to leave the breast as a warm covering for the thorax until the final stage of the operation. The incision permits free exposure, including the subscapular space, which is sometimes neglected; does not run on to the arm or through the axilla, in which situations a contracting scar may interfere with the functions of the arm or press on the blood-vessels and the nerves; and, with extensive undermining, can almost always be closed. When primary closure cannot be obtained the raw surface is covered with pedunculated flaps from the abdomen and the back. Owing to the situation of the incision a second opening is not needed for drainage, and the dressing of the wound is simplified. The drain, when employed for lymphorrhœa, is removed at the end of two days, and never replaced. Leaving the wound open and prolonged drainage mean infection and much fibrous tissue.

An incision, skirting the upper margin of the breast, is made from a point on the edge of the sternum farthest from the growth and on a level with the nipple, to a point on the same level at the posterior axillary fold (Fig. 1). Towels, which are not shown in the illustrations, are attached to the edges of the incision, so as to exclude completely the skin from the field of operation. Parenthetically we may state that in order to avoid fatigue of the eyes and, especially in class work, to bring the operative field into greater relief, we employ, following the advice of Sherman, black, instead of white, sheets and towels for all operations. The skin is undermined from the incision to the clavicle and the head of the humerus, and from the sternum to the posterior

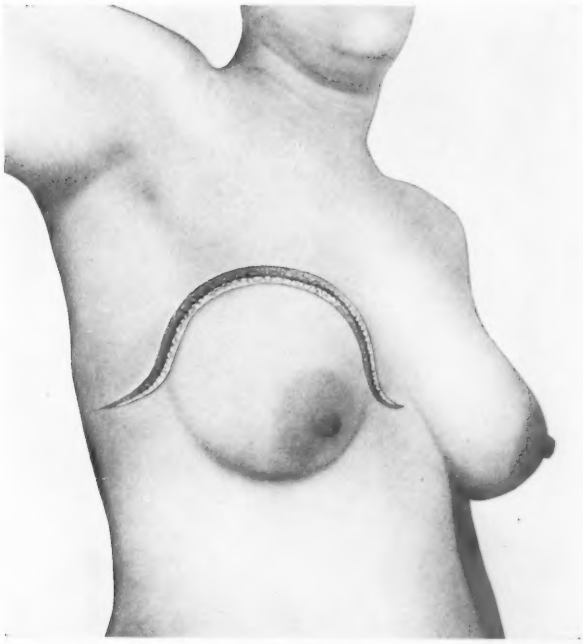

FIG. 1.—Primary incision. The towels which should be attached to the margins of the wound are not shown.

FIG. 2.—Dissection of axilla.

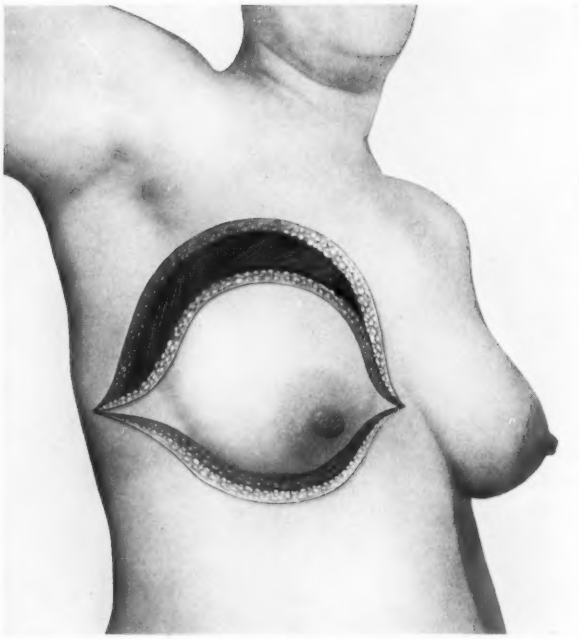

FIG. 3.—The lower incision is made after evacuation of the axilla.

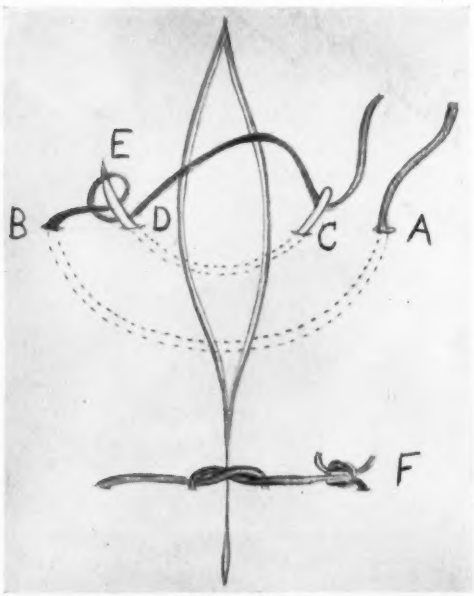

FIG. 4.—Combined retention and coaptation suture. The needle is inserted a couple of inches from the edge of the wound (*A*) and brought out at a corresponding point on the opposite side (*B*). It is then reinserted close to the wound (*C*) and, on emerging from a corresponding point on the opposite side (*D*), is passed through the loop *E*. When the suture is tied (*F*) the edges of the wound are held firmly together and inversion of the skin does not occur.

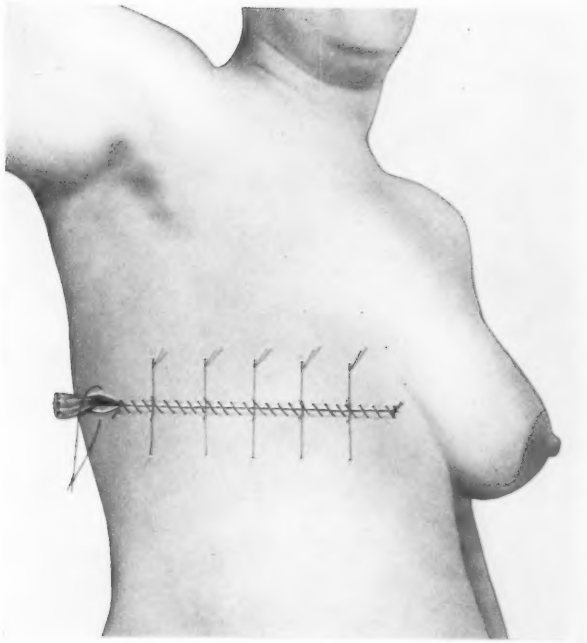

FIG. 5.—Incision closed.

axillary fold. The clavicular is separated from the costal portion of the pectoralis major, and the tendon of the latter severed close to the humerus. The costocoracoid membrane is divided, and the pectoralis minor cut at its point of insertion. With a self-retaining retractor of the Balfour type, and a smaller retractor held by an assistant, the entire axilla is exposed for evacuation (Fig. 2), which progresses from above and within downward and outward, as in the Meyer operation. The vessels supplying the breast are divided between ligatures. The subscapular vessels are tied at each end, and, with the environing areolar tissue, pushed toward the median line, thus laying bare the latissimus dorsi, teres major, subscapularis, and serratus magnus. The ends of the original incision are joined by a cut which skirts the inferior margin of the breast (Fig. 3), and the skin undermined to the level of the lowest portion of the costal arch, or even lower. Through this incision one may remove, as suggested by Handley, the deep fascia over the upper portion of the abdominal muscles; we have not adopted this procedure as a routine measure. Next the breast is turned toward the opposite side of the body, the origin of the pectoralis minor cut, the perforating vessels seized before division, and the mass removed by severing the costal origin of the pectoralis major. The wound is irrigated with hot salt solution, and closed with several combined retention and coaptation sutures of silkworm gut (Fig. 4), and a continuous suture of celluloid thread, except at the axillary end, where one suture is left untied, to provide an exit for a gauze drain (Fig. 5), which is removed in 48 hours and the suture tied.

The arm is not bandaged, and the patient is allowed to put it into any position she desires. Œdema of the arm immediately following operation we regard as a favorable sign; it indicates that the operation has been thorough, that all the lymphatic structures in the axilla have been removed, and the lymphatic drainage of the arm completely interrupted. It usually disappears in from two to four months, but may last longer, and indeed be permanent. Œdema appearing after an interval is due to pressure on the axillary vein by a cicatrix, by a recurrent growth; to a neoplastic invasion of the vein; to venous thrombosis; to a tardy lymphangitis or lymphthrombosis; hence is not always, as is sometimes thought, a premonitory sign of early dissolution.

We have employed the method described above during the past five years, in 40 cases, and our colleague, Professor John H. Gibbon, has, during the past four years, used the same procedure in 47 cases, making in all 87 amputations of the breast by the transverse incision.

NON-CALCULOUS OBSTRUCTION OF THE UPPER URETER*

By Charles H. Peck, M.D.

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surgeon to the roosevelt hospital

In September, 1906, I was confronted by a surgical problem which caused me much anxiety and which I failed to solve in a satisfactory manner. A woman fifty-four years of age came under my care with complete obstructive anuria of 48 hours' duration. Her left kidney had been removed seven months before for sepsis, following two previous operations for nephrolithiasis. Several attacks of partial obstruction of the right ureter had been relieved spontaneously in the interval, the attack in which I first saw her being the first absolute closure.

Emergency nephrotomy was followed three weeks later by an attempt to relieve the non-calculous valvular obstruction at the junction of pelvis and ureter by a plastic operation similar in type to the Finney pyloroplasty. After much effort and many subsequent attempts to pass ureteral catheters both from below and above, failure had to be acknowledged, and permanent lumbar drainage established, with proper apparatus for collecting the urine. The patient lived in comparative comfort until October 23, 1907, when she died following an operation for infection of the nasal sinuses, performed by another surgeon.

In February, 1910, a man thirty-nine years of age presented himself with a history of frequent attacks of right renal pain, dating back for about a year. Cystoscopy showed diminished right renal function, and radiographs were negative.

Operation showed a tense hydronephrosis of moderate size, with a high ureteral implantation and hooding of the posterior part of the pelvis in such a way as to cause valvular obstruction of the upper ureter. The obstruction was complete at the time of the operation and pressure failed to force urine from the pelvis into the ureter. Nephrotomy showed much thinning of the cortex with dilatation of the calyces, and a single calculus, the size of a pea, which was not at that time lodged at the entrance to the ureter, but was free in the sac. After collapse of the sac a good sized spiral metal ureteral probe was passed through the opening in the cortex, into the ureter and on to the bladder without meeting obstruction. A diamond-shaped segment of the re-

* Read before the American Surgical Association, June 11, 1915.

dundant posterior wall of the pelvis was then excised, and, after inspecting the ureteral orifice, the defect was carefully sutured with two tiers of fine chromicized catgut in such a way as to secure normal relations at the pelvi-ureteral junction.

Remembering my unfortunate experience with the former case it occurred to me that it might be well to leave the ureteral probe in position to act as a sort of splint, and to guard against kinking or angulation at the pelvi-ureteral junction while the replaced kidney was becoming fixed in its new position. The metal probe was therefore again passed through the opening in the cortex of the bladder, with a small tube drain alongside, reaching the kidney pelvis; a mattress suture of catgut through the kidney substance was placed about both and tied just tight enough to control hemorrhage; the kidney was replaced and the wound closed to the exit of the drain and probe, the latter being bent to the surface of the body and secured with adhesive straps.

The probe was removed at the end of twenty-four hours; the tube drain at the end of four days, and the patient made an uneventful recovery. Post-operative pain while the probe was in place was perhaps somewhat greater than after an ordinary nephrotomy, but not excessive, and no apparent harm of any sort was caused by the presence of the probe.

Subsequent cystoscopy, nine weeks later, showed secretion from the right ureter normal in amount, appearance and rate. The patient has remained well, with no return of symptoms, for more than five years. The right kidney, damaged as it was by over-distention, was saved as a functionating organ.

The outcome of this case encouraged me to apply the principle of "splinting the ureter" to subsequent cases, and I have performed the operation fourteen times.

Four of the cases (including the one reported) had distinct hooding of the pelvis with complete valvular closure at the pelvi-ureteral junction, two with a small calculous and two without. In three cases diamond-shaped segments of the posterior pelvic wall were excised, the defect being sutured in such a way as to bring the ureteral implantation into correct relation with the pelvis, and in one the pelvis was plicated without excision of a segment to produce the same effect. In all except the first case ordinary ureteral catheters of large size were used as splints instead of a metal probe.

Late reports on these four cases show them to be in good condition, without recurrence of symptoms, for five years four months, three

years five months, three years seven months, and one year five months, respectively.

Two cases had mobile kidneys with marked dilatation of the pelvis without definite hooding or valvular obstruction. In these the obstruction was probably due to kinking of the upper ureter dependent on the mobility of the kidney. Insertion of the ureteral splint and nephropexy was the procedure adopted in these cases without resection or plication of the wall of the pelvis.

Two cases had definite cicatricial stricture of the ureter 1 inch and 1½ inches, respectively, from the upper end, one of them having a single small stone and the other 26 very minute calculi, one of the latter impacted just above the stricture. These strictures were carefully dilated with metal probes before the ureteral catheter was left in place.

One case had kinking and obstruction of the upper ureter following a nephrotomy performed for calculus four years previously, due to post-operative adhesions.

One case had an S-shaped kink in the ureter without much dilatation of the pelvis, but with intermittent attacks of pain of an ureteral type.

Two cases had chronic pyelitis of a mild degree, with attacks of pain suggesting intermittent obstruction, dating back two and ten years, respectively. In neither case was there much dilatation of the pelvis, nor could the presence of an actual obstruction be demonstrated. Both of these cases were drained to the pelvis of the kidney in addition to having the ureteral splint placed. In one case the splint was placed at a secondary operation following excision of a tumor of the bladder which involved the right ureteral orifice, for development of kidney pain and ureteral obstruction, the idea being to keep the lower ureteral orifice patent during healing of the bladder wound. For several reasons I doubt the wisdom of this procedure, and do not advocate it, although it seemed to be followed by at least temporary relief in the case referred to.

I have received reports from all the fourteen cases cited, and all have remained well since the operation, and permanently relieved of their former symptoms. None have required secondary operations. The cases have seemed worthy of report, to call attention to the use of this method of splinting the ureter by leaving a firm ureteral catheter in place for a few days after operation, thus guarding against kinking or angulation of the ureter or pelvi-ureteral junction while kidney and

ureter are becoming fixed in their new position after operation. I believe that in a number of cases of moderate hydronephrosis due to obstruction of the upper ureter, the use of this method, combined with a plastic operation on the pelvis of the kidney, with nephropexy for movable kidney, relief of constricting bands or vessels and so forth, will result in saving a functionating organ in some cases which might otherwise come to secondary nephrectomy.

CORRESPONDENCE

DR. DEPAGE'S LETTER OF APPRECIATION TO AMERICAN SURGEONS

MY DEAR COLLEAGUES:

I have received from a large number of you, and notably from the Committees which you have formed, the most touching tributes of sympathy and of condolence for the catastrophe of the Lusitania in which my wife lost her life.

These tributes are so numerous and so unanimous, that I wish to express to you publicly my appreciation of them. I address myself to you, my dear colleagues, as the authorized representatives of the humanitarian sentiments which so honor the great American Nation.

You all know, as I wrote to you when my wife left for America, for what purpose she accepted the mission which the Red Cross confided to her. In the presence of the unexampled miseries of which we have been the prey, she had resolved to solicit your fraternal assistance. You gave her that largely, I should say "joyously," if the word could be pronounced in these times.

The letters my wife wrote to me in the course of her mission told me how you worked for her and revealed to me the extent and generosity of your projects for our wounded. Your hearts were open to our appeal; your Country did not wait to come to our assistance. Powerful America wished to take under her protection our little people, tortured but always valiant.

My great sorrow does not permit me to reply as I wish I might to each one of you. Only to-day have I been able to measure—thanks to the letter of your compatriot, Dr. Houghton—the extent of the gratitude I owe, to him first for having risked his life in trying to save that of my wife, and after that to you all for your devoted help in our common work.

Under the strain of my emotion, the sentiment of thankfulness is the only one to which at this moment I am able to give expression. Permit me to do so with all my heart.

ANTOINE DEPAGE.

June 25, 1915.